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CA

Bulletin of

Cancer Progress

out of the shadows

At the recent meetings of the American Association for Cancer Research, 10 of the 25 sessions were given over to cancer chemotherapy. Let us hope that out of this intensive, over-shadowing effort to find compounds which will cure cancers, success will soon be achieved. Realistically, progress cannot be measured by the yardstick of chemically cured cancers today. There are none.

In the shadow of this gigantic effort are the undramatic cancers which are now being prevented before they begin. In this category, in the United States alone, are the following: conservatively hundreds of cases of lung cancer among those who have already given up cigarette smoking, and some others cured because they were discovered early enough; countless cases of cervical cancer which, some evidence suggests, were prevented by circumcision and good genital hygiene, and thousands more cured in early stages because of routine cytologic examination of cervical smears; countless cases of stomach, skin, bladder, scrotal and lung cancers prevented by the avoidance, wittingly or unwittingly, of carcinogenic factors to which man has been exposed in his occupation or elsewhere in his environment.

These *unborn cancers* must come *out of the shadows* and light the way for prevention as the most effective means of controlling these diseases today. At the present rate of increase millions will die of lung cancer alone in the next few decades unless adequate prevention is instituted.

The challenge is to the individual physician to decide how he can arrange to see his patients when their diseases are *preventable* and *curable*—even before symptoms appear—instead of after they become *incurable*.

DEAN F. DAVIES, M.D., Ph.D.

Cover—

Ancient symbols depicting family life—
Upper left: man
Lower left: woman
Center and upper right: The family, man with his wife and children.

Cover design by Fred Rothberg, New York.

NEWSLETTER

MARCH-APRIL, 1960

Boucot (Women's Medical College, Philadelphia) in her study of smoking in 6000 men over 45 observes that the highest rate of coughing occurred among cigarette smokers. In the heavy cigarette smokers 45 per cent were coughers; among heavy pipe smokers the rate was 28 per cent, and among heavy cigar smokers 23 per cent. Eighty three of 92 lung cancers occurred in cigarette smokers; only 8 cases of lung cancer were found in cigar or pipe smokers. (One case of lung cancer appeared in the nonsmoking group.)

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Overholt (Overholt Thoracic Clinic, Boston) finds in his series of 2007 cases of lung cancer that when the cancer is localized, the five-year survival rate after surgery is 33 per cent, the three-year survival rate is 53 per cent. When there is metastatic involvement of mediastinal nodes, the five-year survival rate after surgery is 20 per cent, the three-year survival rate is 33 per cent. He offers strong support for exploratory operations of the lung.

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New experiments on rats and mice lend support to the theory that a tumor may elaborate an agent that is transmitted by way of the blood stream which broadly affects the physiology of the host bearing the tumor. Cerecedo, Bresnick and Schubert (Fordham University, New York) used myeloid leukemia in the mouse and Jansen sarcoma and Murphy-Sturm lymphosarcoma in the rat.

Changes observed in nucleic acids, potassium, hemoglobin, total blood solids and whole blood specific gravity in a tumor-bearing animal are not of a permanent nature but are reversed when tumors undergo regression. Apparently, the agent responsible for the changes disappears with the regression of the tumor.

Schneider (Washington University School of Medicine, St. Louis) points out that in selected patients with ulcerative colitis or familial polyposis a two-stage operation ultimately permitting sphincter control can be performed instead of a permanent ileostomy. The operation was successfully done on six patients.

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Salaman (London Hospital Medical College) finds more and more reports are showing that newborn mice, when inoculated with cell-free filtrates of leukemic tissue, develop not leukemia but solid tumors instead. His experiments show that in 15 out of 23 mice inoculated when less than 17 hours old 40 tumors appeared, the first after 11 weeks, the latest after 23 weeks. The tumors were subcutaneous tumors of the neck or of the trunk, mammary carcinoma, fibrosarcoma and fibromyxosarcoma. Metastasis to the lungs was observed in a mouse bearing tumors of the mammary and salivary gland type. So far, no leukemia has developed in any of these inoculated mice, although the filtrate came from a homogenate of leukemic tissue. The mice inoculated were of a different strain from the tissue used in the inoculations. The leukemic tissue came from a mouse of the AKR strain, and the mice injected were C3H strain.

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Birch and Baker (Cornell Medical Center, New York) have reviewed the records of 1480 children to determine the effect of repeated fluoroscopic examinations and have done a long-term follow-up study of these patients with reference to the incidence of all types of neoplastic disease and to the congenital abnormalities in the progeny. They found that there was no statistically significant difference in stillbirth rate from that of the general population and that the rate of congenital defects was similar to that of the general population. They state, however, that these results should not be construed to mean that radiation entails no risk, but that the risk to the individual patient was too low to be observed in a population of this size.

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ARTICLES IN *CA* ARE INDEXED IN CURRENT LIST OF MEDICAL LITERATURE AND QUARTERLY CUMULATIVE INDEX MEDICUS, AND SOME ARE ABSTRACTED IN CHEMICAL ABSTRACTS, BIOLOGICAL ABSTRACTS, EXCERPTA MEDICA AND ABSTRACTS OF WORLD MEDICINE.

Address all correspondence to
RAYMOND B. GRIFFITHS, M.D.
Associate Editor
American Cancer Society, Inc.
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a glance . . .

one-minute abstracts of the literature on cancer prevention

Cigarettes and Oral Cancer

Study of the records of 40 women with oral cancer in two Chicago hospitals in a five-year period, showed that the rising incidence of this disease is associated with an increasing use of tobacco and suggests a causal relationship. A consistent finding was history of cigarette smoking of long duration. There were 6.55 times as many men as women with oral cancer in the same period at those two hospitals, but there has been an increase in the proportion of women with this disease. Toward prevention of oral cancer, the physician should educate his patient to avoid smoking, to seek early medical advice concerning any abnormality in the mouth, to practice self-examination, careful oral hygiene and to avoid chronic dental infection, inflammation and badly fitting dentures. The dentist should always be on the lookout for early lesions such as benign growths and leukoplakia.

Dalitsch, W. W., and Vazirani, S. J.: Oral cancer in women: a study of the increasing incidence. Am. J. Surg. 98:869-874, Dec., 1959.

Cancer Prevention in 1970

One may prophesy in the field of respiration that big strides will be made in the knowledge of the etiology of bronchitis; some of the viruses causing the initial damage will have been isolated and a beginning made on the possibility of effective therapy. What is less likely, of course, is that the government will have taken effective measures to reduce the air pollution which helps the bronchitic to his grave, so that we will continue to have the paradoxical situation where silicotic and bronchitic miners are encompassing not only their own ends but that of many of their fellow citizens. Cancer of the lung inevitably will be an even more frightening cause of death and an eminent statistician will still be saying that it is because one is going to develop cancer of the lung that he chooses to smoke. The cigarette manufacturers will probably still be endorsing this view. It is possible that the domestic economy of the country will be rocked when it is discovered that a dish-washing detergent is a major cause of cancer of the bowel.

Peart, W. S.: Probable and improbable advances in medicine to be expected in the next ten years. [Editorial.] St. Mary's Hosp. Gaz. 66:2, Jan.-Feb., 1960.

Cancer of the Lung

When a hint that surgical successes are few creeps into the literature, it is the fash-

ion to counter it by a call for earlier diagnosis, thus creating the impression that this will correct the position. The author does not believe that earlier diagnosis of lung cancer will increase the surgical "cures" to a really significant percentage. The surgery of carcinoma of the lung is depressing. The idea that more extensive operations or more powerful x-ray machines will go an appreciable way towards the solution of the problem seems absurd. Surgery is successful in approximately 1 per cent of all cases of lung cancer. Even if earlier diagnosis could increase the successes threefold, an optimistic estimate, they would still form only 3 per cent of the total. Various sorts of atmospheric pollution, including tobacco smoke, play an important part. Propaganda to urge young people never to take up smoking and support of measures to minimize all forms of atmospheric pollution in cities and factories should receive our wholehearted approval.

Hayward, J.: Some observations on the pathology and treatment of carcinoma of the lung. M. J. Australia 1:14-17, Jan. 3, 1959.

Cure, Prevention and Education

Until the cause or causes of cancer are known cure will seldom be achieved. Overall view of the adequacy of treatment, by surgery, radiotherapy, chemotherapy, serotherapy and psychobiological methods, at the moment presents a very dismal picture. Prophylactic measures designed to prevent a person from getting cancer are of great importance. Because of articles in lay magazines, "education" spread forth by the satanic television set, reports of ultraradical operations and the patient's natural desire for cure, it is difficult to tell patients with certain types of cancer that they cannot be helped by operation. Surgery alone has reached the stage at which no great advance in method can be expected, but its use along with radiotherapy and chemotherapy is promising. Similarly, radiotherapy is increased in effectiveness when certain drugs are used simultaneously—nitrogen mustards, antibiotics, etc. The new method of perfusion with high concentrations of chemotherapeutic agents may prove valuable in localized cancer. Serotherapy may be expected to yield effective results when the causes of cancer have been better elucidated. Perhaps some people develop antibodies against a possible cancer virus or have hormonal changes which lead to death of malignant cells. The fact that the body sometimes knows how to kill cancer may some day show the way to a method by which all cancers can be killed—or even prevented. Cancerophobia is a powerful new disease, insidious, contagious and crippling and its increasing incidence is greatly contributed to by the medical propagandists who use the weapon of fear in their relations to the public. Distilling knowledge about cancer into people will do no good to their mental health and may cause great suffering. Some education about cancer is necessary —so that there will be avoidance of those factors known to be liable to initiate cancer growth, such as occupational hazards, radiation, cigarettes, clay pipes and atomic bombs. Aside from (1) examination of cervical smears for carcinoma in situ and (2) chest x-ray examination, bronchoscopy and examination of the sputum for malignant cells in cases of persistent pneumonia, no cancer prophylactic procedures can be recommended. Routine medical check-ups on healthy individuals which involve thorough physical examinations, x-ray examinations of the whole body, bronchoscopy, cystoscopy, proctoscopy, coloscopy, etc., as are often recommended, should be discouraged since the procedure is more likely to breed neuroticism than complacency. [*See following abstract.*—ED.]

McKendrick, J.: The treatment of cancer. Res Medica 2:25-30, Autumn, 1959.

Informing the Public

An editorial leader disagrees with some of the statements in the article abstracted above. In addition to the need for control of etiologically significant factors, which

requires active and informed public opinion, there is a need for earlier diagnosis of cancer. The most important advances of the immediate future in this field will be diagnostic rather than therapeutic. Early diagnosis rests upon the speedy reporting of significant symptoms which should be known to the potential patient who must be given every encouragement to consult medical advice with least possible delay. There is a risk that this might lead to a nation which takes its temperature when it cleans its teeth, weighs itself when it washes and castigates the waitress for serving a portion over-rich in cholesterol esters, but the public is neither so foolish nor so ignorant as some seem to believe. The results of the general public's getting its medical information from women's weeklies and other lay publications do not seem to be unduly demoralizing. People afflicted with uncertainty and fear by reason of medical knowledge are those who have a predisposition to hypochondriasis, and might be converted to worrying about what might conceivably happen, instead of about what most decidedly will not.

Anon: Medical education—for the public. Res Medica 2:22-23, Autumn, 1959.

Early Lung Cancer

In approximately 270,000 annual physical examinations, including x-ray examination of the chest, in the Navy and Marine Corps between 1950 and 1957, 81 cases of lung cancer were found. Of these, 26 were discovered on routine check-up. Thirteen of these 26 were symptom-free. The other 13 had symptoms varying from minimal ones, such as recent nonproductive cough or change in a chronic cough, to symptoms and signs of moderately advanced superior vena caval obstruction. Of the 13 patients without symptoms, all were operable, all but one resectable and three of the nine diagnosed between 1950 and 1954 have survived five years or longer. The fact that 13 patients had symptoms and had not previously sought medical advice shows the need for continuing education in the early symptoms and their significance. Not one of these 13 lived three years. It is suggested that examinations be done more frequently than once a year in individuals over 50 years of age, the period in which bronchogenic carcinoma approaches its peak incidence. The most significant contribution of the annual examination in respect to lung cancer is the detection of this group of tumors before symptoms have developed.

Brown, R. B.: Value of periodic examinations in detecting early lung cancer. Postgrad. Med. 27:312-316, March, 1960.

Cigarettes and Lung Cancer

Cigarette smoke interferes with normal function of ciliated mucus-secreting epithelium by slowing the rate of mucous flow and changing the quantity and consistency of mucus secreted. Filtration of smoke is capable of obviating this response only when sufficiently effective to retain all particulate matter leaving only gas-phase material to which the term smoke is not applicable. Aqueous solutions of tars collected from filters inhibit mucous flow as does cigarette smoke. Accumulation and retention of particulate matter on the bronchial epithelium is facilitated by these demonstrated effects of cigarette smoke. This suggests a role for cigarette smoking in the pathogenesis of pulmonary cancer.

Falk, H. L.; Tremer, H. M., and Kotin, P.: Effect of cigarette smoke and its constituents on ciliated mucus-secreting epithelium. J. Nat. Cancer Inst. 23: 999-1012, Nov., 1959.

Carcinoma of the Lungs

Results of operation for carcinoma of the lung confirm the rationality of pulmonary resection. Excision was performed in 195 of 628 patients with lung cancer seen during a 20-year period. The operative mortality was about 10 per cent and approximately 28 per cent of those surviving operation lived five years or more. The long interval between onset of symptoms and the beginning of treatment can be shortened only by increasing awareness of patient and physician. High voltage radio-

therapy does not appear to prolong life or achieve significant palliation.

Boyd, D. P.: Carcinoma of the lung; a review of 628 cases. S. Clin. North America 39:677-681, June, 1959.

Preventable Cancer

Ten or 15 years ago the concept of early cancer was based upon size and duration of the primary lesion and the extent of secondary spread. At present the prevailing idea of early cancer is that it is curable or at least controllable for a long period. Consideration of early cancer includes carcinoma in situ, or preinvasive cancer, and even the antecedent precancerous changes and background conditions which result in irreversible cellular changes leading to autonomous and invasive reproduction of cells. Macdonald's biologic predeterminism was one of the first indications of a shift of view toward early cancer. The background reasons for the modicum of truth expressed in the term should be diligently sought, and the concept should not be used as an excuse for inadequate treatment. If cancer is apprehended in the tort stage rather than in the stage of biologic felony, the revolt against the cellular community is more easily contained. In assessing earliness of cancer, microscopic identification is one important factor. A large papillary breast cancer is more curable than a much smaller undifferentiated ductal carcinoma. Other factors modifying the course of breast cancer are menopausal status, physiological steroid milieu and many others, known and unknown, grouped under the term host resistance. Instances of spontaneous regression, the production of immunity to transplantable tumors in animals and the demonstration of tumor cells in the peripheral venous blood indicate biologic relationship between tumor and host that should be investigated by immunogenetic and immunochemical methods. An early cancer, then, cannot be defined simply by its physical and temporal extent. Carcinoma in situ has been recognized in many epithelia—skin, lip, oral cavity, pharynx, esophagus, vulva, vagina, uterine cervix, anus and bronchus. Most of these lesions will undergo inexorable maturation into invasive cancer. Among lesions recognized or suspected as precancerous are senile keratoses, leukoplakia, Plummer-Vinson syndrome, atrophic gastritis, gastric polyposis, polyps of the colon and urinary tract papillomatosis. The disciplines of virology and immunology are becoming of great importance in studying the basic causes of, and reactions to, cancer. We can now start seriously to plan prevention rather than cure of cancer. The most important aspect of cancer management will some day be prophylaxis. Early cancer, then, may be defined as preventable cancer.

Slaughter, D. P.: What is early cancer? Postgrad. Med. 27:271-273, March, 1960.

Pathologic Pulmonary Physiology of Smokers

The pulmonary physiology of 14 persons who had never smoked was compared with that of 14 who smoked 20 or more cigarettes daily for a mean of 18 years. The subjects were selected so as to be similar as regards background history, body surface, height and age, and they did not have signs or symptoms of lung disease. Measurements were taken of vital capacity, timed expiratory capacity and maximum breathing capacity. Arterial samples were obtained and the pulmonary-membrane diffusing capacity, pulmonary diffusing capacity, blood oxygen tension and lung volume were subsequently calculated. It was found that in heavy smokers the time expiratory volume, total lung capacity and maximum breathing capacity were decreased. The ratio of the residual volume to the total lung volume was increased in these individuals. The total lung diffusing capacity and membrane diffusing capacity were decreased in persons who had smoked more than one package of cigarettes per day for 18 years. These data indicate that cigarette smoking decreases pulmonary function and that most smokers have some degree of pathologic change in lungs or bronchial structures which causes them to have abnormal pulmonary function.

Wilson, R. H.; Meador, R. S.; Jay, B. E., and Higgins E.: The pulmonary pathologic physiology of persons who smoke cigarettes. New England J. Med. 262:956-961, May 12, 1960.

Keeping up

Cutaneous Precanceroses

Some recognizable lesions of the skin are forerunners of cancer so frequently that their removal is a valuable prophylactic procedure. Among these precanceroses are leukoplakia; hyperkeratoses — senile and those caused by irradiation, tars, hydrocarbons and arsenic; benign basal cell epitheliomas; and sebaceous and epidermoid cysts. In kraurosis vulvae or penis, cancer occurs only when leukoplakia supervenes and subsequently becomes malignant. There is no sharp line dividing precancer from cancer in skin lesions. The warning signs of increased rate of growth, rapid hyperpigmentation, increased scaling, inflammatory change, fissures, ulceration, bleeding, etc., are observed both before and after there is microscopic evidence of cancer. The entire precancerous tissue should be removed, not just a single lesion or a small area. For destruction or removal of lesions the following procedures may be used: chemical, thermal (heat or cold), electrical currents of high frequency, excision by scalpel or curette, and irradiation by x ray or radium. Keratoses are best destroyed by electrosurgery. It is time-saving, convenient, inexpensive and gives good cosmetic results as well as an excellent rate of cure.

Lynch, F. W.: Recognition and management of the cutaneous precanceroses. Postgrad. Med. 27:337-348, March, 1960.

Oral Leukoplakia

Leukoplakia of the oral mucous membrane is a precancerous lesion. It is a chronic inflammation occurring on the tongue, cheeks, lips, palate or vocal cords. Deficiency of vitamin A and excessive use of alcohol and tobacco are etiologic factors. Smoking, chewing and using tobacco as snuff are considered to be causes of leukoplakia, but since leukoplakia occurs also in nonsmokers tobacco is not the only cause. Poor oral hygiene and decayed teeth may contribute to the formation of leukoplakia. Since alcoholics, male and female, are usually also heavy smokers and poorly nourished, it may be the concomitant avitaminosis A that is the true etiologic factor [like avitaminosis B in alcoholic neuritis]. The author cites a patient with leukoplakia of the vocal cords and tongue who for years had smoked four packs of cigarettes a day and for the past year consumed a bottle of whiskey daily. No cancer was found in the larynx or oral cavity. The patient discontinued the use of tobacco and alcohol. The leukoplakia of the larynx has nearly disappeared and that on the tongue was excised. Frequent follow-up examinations are recommended. Leukoplakia should be treated first by removal of the causal factors, if known, then by improvement of oral hygiene, treatment of dental sepsis, removal of alcohol and tobacco, maintenance of a well-balanced diet, elimination of constipation—all these before the definitive treatment of the lesion itself by complete surgical excision or desiccation by electrocautery. Radiation therapy in any form is contraindicated.

MacComb, W. S.: Leukoplakia of the intraoral cavity. Postgrad. Med. 27:349-355, March, 1960.

Early Thyroid Cancer

Many surgeons feel that most nodular goiters should be removed. This is the rea-

with Cancer

son most early thyroid cancers are found by the pathologist. Not all pathologists are adept at giving a diagnosis from frozen sections; in fact, experienced pathologists sometimes disagree on whether a thyroid lesion is benign or malignant even after microscopic examination of fixed sections. Keen interest in the use of frozen sections develops a high degree of accuracy in their use. Some surgeons favor immediate prophylactic neck dissection; others, including the author, reserve neck dissection for patients with clinical evidence of lymph node spread. Between 1946 and 1959, 142 cancers of the thyroid gland were operated upon. Of these, 97 (68 per cent) were first diagnosed by the pathologist. Forty-five were clinically self-evident cancers. Once the diagnosis of malignant change is established, the surgeon must follow an immediate program of radical surgery or of watchful waiting and keep all such patients under careful surveillance. Cancer of the thyroid can be one of the most malignant and enigmatic of all tumors.

McClintock, J. C.: Early treatment of cancer of the thyroid gland. Postgrad. Med. 27:416-421, March, 1960.

The Precancerous Lesion

A lesion is to be thought of as precancerous if cancer is added more often to it than when it is not there. But finding a lesion to be precancerous doesn't explain very much concerning the cause of cancer. There is no direct, uninterrupted line from normal to precancer to cancer. A lesion may look quite like a malignant tumor without being either cancerous or precancerous. For example, keratoacanthoma is a benign lesion of the skin difficult to distinguish from squamous cancer. Benign seborrheic papillomas resemble basal cell carcinomas. The benign calcifying epithelioma of Malherbe is confused with squamous carcinoma, but this lesion is not precancerous. In mucous membranes the benign granular myoblastoma resembles squamous carcinoma. Cutaneous lupus may be precancerous, especially when irradiated. Precancerousness is something more than a mere pattern under the microscope. The placenta is the crowning example of resemblance to cancer with absence of even precancerousness. To distinguish early normal placenta from choriocarcinoma requires second sight. The placenta destroys, invades, derives its blood supply from "abnormal" means, invades vessels and disseminates—all without being cancerous or precancerous. Oral leukoplakia and laryngeal pachydermia, although more innocent-looking than some of the benign lesions, are precancerous. Mammary cancer in pathologically recognizable form may exist within mammary ducts for a decade without infiltrating. The precancerous stage is probably even longer. In the gastrointestinal tract cancer in polyps is overdiagnosed, just as is cancer in situ of the cervix—part of the total enthusiasm for early diagnosis. Forty per cent of villous tumors develop into invasive cancer. Ulcerative colitis is definitely precancerous. The author has seen almost no instances where proof of the precancerousness of peptic ulcer could be absolutely defended. Gastric polyp is a very rare precancerous lesion, mostly in addisonian anemia. Gastric carcinoma in situ, Versé plaques, can exist in precancerous form for many years before becoming clinical cancer. In the lung, carcinoma in situ must

antedate infiltrating cancer but there is no agreement where metaplasia and atypias end and carcinoma in situ begins. Carcinoma in situ is surely the precursor for infiltrative cancer of the cervix. It may take years—up to 13—to become clinical cancer. The lesion may be interrupted without definitive treatment and may recur after a long period. Patients with cervical carcinoma in situ should be followed closely by recurrent investigation and should not be allowed to drift from observation. Polyps and cystic and adenomatous hyperplasia are precursors of endometrial cancer. Papilloma and leukoplakia are precancerous bladder lesions. Among the precancerous lesions of the skin are sunlight keratoses, chemical keratoses, radiation dermatitis, xeroderma pigmentosum, arsenical keratoses, lymphopathia venereum, kraurosis vulvae, psoriasis and lupus. One must know lesion behavior from his own and others' experience to recognize the precancerous state. Mere histologic appearance of tissues and cells is not sufficient.

Stewart, F. W.: The problem of the precancerous lesion. Postgrad. Med. 27:317-323, March, 1960.

Early Cancer of the Face

Cancer of the face is unique in its accessibility for early diagnosis and treatment. Cutaneous cancers constitute 40 to 60 per cent of all types of malignant lesions seen by the family physician. He must remember that there is no "routine" operation or "routine" therapy and that he is dealing with a human being as well as with a tumor. Skin cancers develop more frequently in blond individuals and in those with thin, dry skin. Farmers, ranchers, fishermen and sailors are most frequently affected. Squamous cell cancers often develop on keratotic and eczematoid areas of the nose, ears and cheeks and on areas of postirradiation dermatitis. Ulceration in old burn scars may become malignant. Papillomas and warts, irritated by shaving, rubbing or picking, may become carcinomatous. Contrary to most teaching, the authors regard basal cell carcinomas as elusive, invasive and highly malignant even though they do not metastasize. Rodent ulcer is the most difficult basal cell lesion of the face to eradicate and one of the most dangerous. Since squamous cell carcinomas are very malignant and metastasize early to regional lymph nodes they should be diagnosed and treated early. Any persistent growth on the face, no matter how small, may be cancerous. Results of treatment depend upon how early the patient seeks advice and upon the adequacy and thoroughness of treatment. Excision must be wide and deep enough to encompass all malignant and potentially malignant tissue.

Pickrell, K. L.; Georgiade, N.; Adamson, J., and Matton, G.: Surgical treatment of early carcinoma of the face. Postgrad. Med. 27:406-415, March, 1960.

Early Rectal Cancer

Cancer of the rectum has been shown to develop in apparently normal intestinal mucosa as well as in benign mucosal polyps. It is generally accepted that there is an intimate relationship between carcinoma and benign mucosal polyps of the colon and rectum and that such polyps should be removed or destroyed. An appreciable group of patients with polyps showing early histologic cancer can be treated conservatively by local excision or fulguration. The surgeon's decision for radical treatment is influenced by the presence of induration, fixation and ulceration, usually indicating invasive and clinical cancer. To the pathologist the presence of invasion means cancer; anaplasia and irregularity of architecture without invasion may exist without the tumor's being malignant. For tumors of the rectum showing early histologic cancer without invasion, removal through the sigmoidoscope by high-frequency electric snare or destruction by cautery is usually adequate. For larger tumors at higher levels, local excision by colotomy may be indicated. Local or segmental resection may be required if, at examination through a colotomy incision, the nature of a polyp high in the rectum is questionable after immediate frozen sections. Large, villous tumors

can usually be removed by snare or destroyed by fulguration. Even though local areas of noninvasive histologic cancer are present, abdominoperineal resection or pull-through procedure is seldom necessary.

Swinton, N. W., and Snow, J. C.: Early cancer of the rectum. Postgrad. Med. 27:401-405, March, 1960.

Head and Neck Examination

Cancers of the head and neck are accessible to direct observation by the physician and by the patient and his associates. Accordingly, skin carcinomas of the head and neck are brought to the attention of the physician while they are small, localized and readily curable. Similarly, lesions of the oral cavity are noticed early by the patient or, on account of bad breath, by his associates. Dentists are becoming more alert in noting lesions of the mouth requiring biopsy. Physicians often examine the mouth so perfunctorily as to overlook precancerous lesions and early cancers. Early tumors of the salivary glands and thyroid may often be found by periodic examinations of the asymptomatic patient. The routine physical examination rarely discloses early cancer of the larynx, pharynx, accessory sinuses or esophagus; but careful questioning regarding nasal discharge, hoarseness, difficulty in swallowing, etc., may elicit justification for x-ray studies, laryngoscopy and other diagnostic procedures. Discovery of masses in the neck leads to studies to establish a diagnosis of lymphoma, sarcoma or of metastatic carcinoma from a distant site. Careful inspection and palpation, together with interrogation, should disclose a very high percentage of cancers of the head and neck in an early, curable stage.

Taylor, G. W.: Value of periodic examination in head and neck cancer. Postgrad. Med. 27:295-296, March, 1960.

Early Cervical Cancer

Early cancer of the cervix includes carcinoma in situ, carcinoma in situ with microscopic invasion and Stage I invasive carcinoma. The first step in management is to determine the extent of the disease in area and in depth by the following procedures: inspection, palpation under anesthesia, Schiller iodine test, biopsy, cystoscopy, proctoscopy and x-ray examinations of the urinary tract, the lungs and the skeleton. For carcinoma in situ adequate treatment consists of hysterectomy which includes the entire cervix and a fully circumferential vaginal cuff. When preservation of fertility is desired, local excision, conization and cauterization may be used, but this procedure is less apt to be effective in control. Repeated cytologic and biopsy tests must be normal before it is safe to permit conception. When the patient is pregnant endocervical curettage and cone biopsies must exclude invasive cancer, and then further treatment can be delayed until after delivery. Such manipulation of the cervix does not increase the incidence of miscarriage. Radiation treatment for carcinoma in situ is justified only when hysterectomy carries a prohibitive risk. Carcinoma in situ, adequately diagnosed and treated, should always be cured. Carcinoma in situ with microscopic invasion and Stage I invasive carcinoma are treated in the same way. The surgical procedure includes en bloc removal of the uterus, cervix and vagina, dissection of the pelvic walls and floor, with preservation of the bladder, ureters and bowel. Adequate radiation to this block of tissue cannot be delivered by any technique of local application alone. The dose must be augmented by external radiation. Surgical and radiation failures are usually those cases which are in fact more extensive than Stage I. It is justifiable to expect cure in every early case; every failure should be carefully studied.

Ulfelder, H.: Treatment of early cancer of the cervix. Postgrad. Med. 27:398-400, March, 1960.

Precancerous Thyroid

A large percentage of thyroid cancers has its inception in pre-existing adenomas. In Switzerland, the incidence of thyroid cancer was diminished by two-thirds following correction of iodine deficiency in the population. In addition to lack of

iodine the following etiologic factors of cancer of the thyroid have been established: ionizing radiation, thyroid insufficiency from partial thyroidectomy and thiourea and related compounds. All of these goitrogenic factors—except possibly radiation, which acts directly on the thyroid epithelium—interfere with thyroid hormone synthesis, storage and release. Reduction in thyroid output causes increased pituitary production of thyrotropic hormone which stimulates the thyroid epithelium and causes compensatory enlargement of the gland, or goiter. In animals, these goitrogenic factors produce all the histologic changes observed in the human thyroid—simple hyperplasia, adenomatous change, adenoma and metastasizing cancer. It was learned, first in animals and then in man, that some cancers, principally the papillary variety, respond to treatment with desiccated thyroid. The cancerogenic effect of ionizing radiation on the thyroid should exclude radiotherapy of benign conditions of the neck in infants and children. Radioactive iodine has been used for too short a time to permit an opinion concerning its possible cancerogenic effect in adults. With rare exceptions, single thyroid nodules should be removed, especially in the young.

Anglem, T. J.: Precancerous lesions and other conditions of the thyroid gland. Postgrad. Med. 27:366-369, March, 1960.

Cost of Cancer Detection

Almost three quarters of cancers can be detected for twenty-five dollars or less, exclusive of the biopsy fee. The cost of detection is directly related to the accessibility of the body site affected. The more accessible the cancer the more economical its detection and the more likely it is to be discovered early. Such early diagnosis is also economically advantageous to the patient, since less extensive, less prolonged and less costly treatment is required. A skin tumor, for example, may be detected in the physician's office at a cost of a regular office visit plus a ten to twenty dollar fee for biopsy. Costs of several diagnostic methods have been reduced to a point where they may be used as screening procedures in mass examinations. An example is the Papanicolaou cytologic method of detecting cervical cancer. This method was used in Memphis over a four-year period with the detection of four cases of cervical cancer per thousand of the 120,000 women examined.

Clark, R. L., Jr.: Economics of cancer detection. Read at the annual meeting of the American Cancer Society, Oct. 26, 1959. New York, N. Y.

Gastric Precancers

Peptic ulcer, polyps, chronic atrophic gastritis and pernicious anemia are the conditions of the stomach commonly held to be precancerous. Since it is impossible to examine the suspected tissue under the microscope and in the patient simultaneously, there is no incontrovertible proof that transition from one of these benign states to a malignant one ever actually occurs. Such changes are based on presumption rather than fact. It is impossible to say how frequently benign ulcers become malignant. Some estimate as high as 70 per cent and others say never. X-ray examination is the best method of diagnosis, accurate to more than 80 per cent. With the supplemental use of gastroscopy and cytology nearly 100 per cent accuracy of gastric cancer diagnosis is possible. As soon as these examinations confirm a suspicion of cancer immediate operation should be advised. When textbook symptoms of gastric cancer appear, favorable prospects from operation have greatly diminished. Polyps occur in general in the same locations as gastric cancers and like cancer and chronic atrophic gastritis are associated with achlorhydria. In any case of obscure anemia careful investigation of the digestive tract for polyps, ulcer and carcinoma is advisable. Final determination of malignancy of polyps can be made only by histological examination. Surgical treatment is indicated for any polyp which contains carcinoma in situ, or causes symptoms of obstruction, or is associated with gross or occult bleeding, anemia or indi-

gestion of any type. Operation on polyps considered to be malignant requires resection of the stomach because cancer has been known to occur at the site of simple excision of a polyp. Patients with atrophic gastritis, especially if it is accompanied by pernicious anemia, should be checked by x-ray, gastroscopic and cytologic examinations every six months. Gastric cancer occurs three times more frequently in patients with pernicious anemia than in other patients of comparable age. Some say 10 to 20 times. It is advisable to suspect gastric cancer in all patients with pernicious anemia. When the surgeon and the referring physician, after an adequate trial period of medical treatment, agree that there is a reasonable suspicion of malignancy based on appropriate studies by qualified individuals, there should be no delay in resorting to operation.

Boles, R. S.: Precancerous lesions of the stomach; how to treat them. Postgrad. Med. 27: 359-365, March, 1960.

Early Cancer of the Larynx

Lesions of the vocal cords cause intermittent or persistent hoarseness early in their clinical courses but lesions at other sites of the larynx and laryngopharynx are asymptomatic and silent until of considerable size. Early cancer of the larynx, therefore, is detected only in the vocal cords. Cancers confined to one cord, or with limited involvement of the anterior commissure and opposite cord are the most favorable for irradiation therapy. Those causing fixation of one side of the larynx, those with subglottic extension, and those with more than minimal invasion of the ventricle cannot be considered to be early and are unfavorable for treatment by either partial laryngectomy or irradiation. One hundred and ninety-four partial laryngectomies and two patients treated by irradiation are reported. Of the two irradiated patients, one was cured; the other died of cancer of the stomach within two years after treatment of vocal cord cancer. In this group there were 181 males and 13 females between ages 26 and 89. There were 28 cases of carcinoma in situ, 44 of superficial invasive carcinoma and 122 of infiltrative carcinoma. After surgery, five cases were complicated by hemorrhage and 50 by emphysema. Twenty seven of the patients had primary cancers of other sites and 17 died of them one to 12 years following partial laryngectomy. Initial treatment failed in 32 cases (16.5 per cent). Of these, 16 were cured by secondary treatment (surgery or irradiation), 10 died of disease, five are living with disease and one died postoperatively.

Frazell, E. L., and Gerold, F. R.: Early cancer of the larynx. Postgrad. Med. 27:394-397, March, 1960.

Early Breast Cancer

Early cancer may be defined histologically as preinvasive; clinically, as of recent onset; anatomically, as small, freely movable and without evidence of extension by blood or lymph; therapeutically, as amenable to complete surgical excision or successful radiotherapy; prognostically, as having a favorable chance of cure; and biologically, as recent or new in its natural history. Earliness, then, of breast cancer is not measured in months or centimeters alone but must be considered in terms of the broad and comprehensive manifestations of malignancy and metastasis. Cancer of the breast early in time and early in size is more apt to be early in prognosis. The American Cancer Society in its drive for early diagnosis and in its promotion of self-examination of the breast has brought patients under observation earlier. During the period 1935-1945 at Johns Hopkins Hospital about 33 per cent of the patients with operable breast cancer were of Stage I; ten years later this percentage had increased to 45. Prognosis in breast cancer "gets worse as the size of the tumor increases." The most important measurable factor in prognosis is the extent of metastasis. In the author's series, treated by radical mastectomy, the five-year survival rate is 71 per cent without, and 34 per cent with axillary metastases. Average survival for untreated breast cancer is three years; for all treated cases, five years; and for those detected in time and treated early,

13 years. "Only the beginnings of a cancer permit of a cure."—Celsus.

Lewison, E. F.: Value of periodic examination in early cancer of the breast. Postgrad. Med. 27:297-300, March, 1960.

Cancer of Rectum and Colon

At Strang Cancer Prevention Clinic (New York City) from 1946 to 1954, 26,126 examinees underwent complete proctosigmoidoscopic examinations. In this group, who were asymptomatic or had minimal symptoms, 58 (0.22 per cent) cancers of the rectum and colon were found. The rate was 0.18 per cent for women and 0.31 for men. The most common symptoms leading to diagnosis were bleeding and alteration of bowel habits. Many of the tumors were small and lymph nodes were involved in less than 20 per cent. Operations for cure were possible in 96 per cent and 88 per cent of all patients were free of cancer after five years. These results are significantly better than those in patients presenting for diagnosis because of symptoms. Two of the cancer patients had previously had benign adenomas biopsied and diagnosed, had failed to have the tumors removed as advised, and returned, still symptom free, but with cancers at the same sites. In situ changes and early invasive cancer were found in adenomas in 47 additional cases (0.18 per cent). The rate was 0.16 per cent for women and 0.22 per cent for men. Three fourths of these patients were asymptomatic. Cancer can arise in the asymptomatic adenoma found upon routine examination if it is neglected.

Hertz, R. E. L.; Deddish, M. R., and Day, E.: Value of periodic examinations in detecting cancer of the rectum and colon. Postgrad. Med. 27:290-294, March, 1960.

Educating the Laity

Twenty years ago one of four cancer patients survived for five years; now one of three survive. This improvement in results is largely attributable to better therapy, but there is evidence that lay cancer education leading to earlier diagnosis is also a factor. The successful cancer education programs of the American Cancer Society and the American College of Surgeons are based upon persuading people to have physical check-ups and teaching them the cancer danger signals. Since there are not enough physicians to provide semi-annual examinations for the entire population, it is suggested that detection programs be concentrated upon high risk groups, according to age, sex, occupation, socioeconomic status, environment, race, religion, etc. Educational material should be adapted to each specific age-sex group, and then brought to each particular group intensively and frequently, by all media of communication. For example, women who bottle-feed their children should be especially alerted to have more frequent breast examinations than women who breast-feed their children. The American Cancer Society has started another large-scale study (similar to that of lung cancer and cigarette smoking) of the medical histories of thousands of apparently well people with a view to correlating symptoms, beside the usually listed cancer danger signals, with the subsequent development of cancer. This six-year study should yield important data.

Hammond, E. C.: Lay education in cancer. Postgrad. Med. 27:324-331, March, 1960.

Staging and Reporting Cancer

Without standardized staging, therapeutic results of different investigators cannot be compared. Before results can be evaluated patients must be separated into categories according to the stage of the disease when treatment is begun. Patients will benefit enormously when staging criteria shall have been agreed upon and used consistently in reporting results of therapy. The physician will then be able to anticipate with greater accuracy the result he may expect from a given form of treatment for cancer in a patient of a given category or stage of disease. There have been proponents of staging for cancer of various body sites, but international acceptance of any one classification has not been achieved. The Joint Committee for

Cancer Staging and End Result Reporting of the Research Commission of the International Union Against Cancer, composed of representatives of the National Cancer Institute, the American Cancer Society, the American College of Surgeons, the American College of Radiology, the American College of Physicians and the College of American Pathologists, is studying a proposal based on the TNM system (tumor, regional lymph nodes, distant metastases) and will report its recommendation for applying this system to cancers of the breast and larynx with a view to its being adopted internationally. Eventually this TNM system will be extended to the classification of cancers of all the anatomical sites to which it is applicable, including tumors of the lip, mouth, larynx, skin, uterine cervix and breast.

Clark, R. L., Jr.: Clinical staging and proper end-results reporting of cancer. Postgrad. Med. 27:383-388, March, 1960.

"Cause" of Cancer

"Though the light be dim, we shall not despair." Using this text the author reviews, with much insight though little optimism, the current perspectives in cancer research. Koch's postulates have misled us to look for "a cause" of every disease, including cancer in its many varieties. Viruses (exogenous and plasmagenic), chemicals, embryonal nests and irradiation have been postulated as "the cause." Tumor production by chemicals is found in industrial carcinogenesis and represents but a small fraction of total cancer morbidity. Existing evidence suggests that a specific combination of nonspecific factors is responsible for most human tumors. Pressure by the sponsor often leads the cancer research worker to premature and confusing statements. The recent amazing advance in the technological sciences is largely due to freedom in research. Since our prolonged investigation has not yet produced startling results, possibly a group of young minds without preconceived ideas is needed. Pathologists, biochemists, physiologists, physicians and surgeons visualize the problem through the eyes of their own specialties. Cross-linkage should be improved. Current increased training of medical graduates in basic sciences is proving beneficial in cancer research. Demonstrated sporadic spontaneous regressions and complete arrest of cancer indicate the presence of control mechanisms in the body sufficient to overcome the neoplastic process. Investigations of this control mechanism should be one of the long-term objectives in cancer research.

Skoryna, S. C.: Perspectives in cancer research. Canad. M. A. J. 81:982-984, Dec. 15, 1959.

Heredity in Breast Cancer

This report deals with a study of the families of 544 women treated for breast cancer at the University of Minnesota Hospitals and a comparative study of the parents and sibs of their husbands. Similar comparisons were made between the sons' wives and the married daughters of an additional 77 women with breast cancer. Reported cancers and other tumors were verified by medical histories and death records of all parents, sibs and children. Methods of selection, types of control groups and the statistical effects of incomplete information are discussed. It was found that sisters of the group of the 544 patients had breast cancer at a higher rate than the women in the control group, and the daughters of the 77 patients had breast cancer more frequently than their sons' wives. This increased incidence, although small when considered with other investigations, was interpreted to be real. It is, therefore, very likely that genetic factors are operative in the etiology of breast cancer, but they are either so common in the population or depend so much upon environmental factors for expression that it is difficult to demonstrate their effect. This study shows definitely that relatives of breast cancer patients do not have increased incidence rates of cancer of other sites. The entire study illustrates the difficulties of interpreting the genetic background of a common disease strongly influenced by environmental factors. A ten-year follow-up is proposed for obtaining

better evidence concerning the cancer risk in daughters and sisters and concerning the effect of inheritance upon age at onset of breast cancer.

Anderson, V. E.; Goodman, H. O., and Reed, S. C.: Variables Related to Human Breast Cancer. Minneapolis. The University of Minnesota Press. 1958.

Corticoids in Leukemia

The value of steroids in the treatment of leukemia was established by Farber in 1950. Although they are not the hoped-for panacea they have come to fill an important place in the management of the leukemias. Complete remissions have been reported in 82 per cent of a group of children with lymphoblastic leukemia. Adults are relatively refractory to ACTH and cortisone. After relapse, a second remission, if it occurs, is less complete. Leukopenia is not an absolute contraindication to steroid therapy. In myeloblastic, monoblastic and chronic myeloid leukemia steroids should not be used. In chronic lymphatic leukemia cortisone gives less sustained benefit than does roentgenotherapy, but cortisone is indicated in cases where there is a thrombocytopenia or an associated hemolytic anemia. The effectiveness of steroids can be assessed only after adequate doses have been administered for an adequate length of time. In adults initial treatment should consist of 300 to 400 mg. of cortisone daily, of one-quarter of this dose of prednisone or prednisolone, or of 200 units of ACTH. If benefit is to result it is shown within two weeks. When one steroid is ineffective others should be used, and by other routes of administration, before this form of therapy is abandoned. Steroids are of definite value in certain forms of leukemia, especially when their use is integrated with other forms of treatment.

Lewis, S. M.: Cortisone and its analogues in haematology. Postgrad. M. J. 34:340-346, June, 1958.

Treatment of Postmastectomy Lymphedema

Severe and disabling edema of the arm after radical mastectomy was successfully treated in 32 patients by means of a fitted fabric sleeve with inflatable rubber tubes attached to an electrically operated air pump. A nonelastic glove was used to prevent swelling of the hand while the pump was in operation. A timing device on the pump permitted inflation of the rubber tubes for 15 seconds and a collapsing rest of the tubes for 45 seconds of every minute the device was in operation. Treatment was begun with three to four days of intensive pumping for periods of six to eight hours per day. As the swelling diminished, the sleeve was progressively tightened every two to three hours until the arm became nearly normal in size. The arm was then measured for an elastic sleeve to be worn when the pump was not in operation or no longer needed. The pumping device can be reapplied at intervals as needed to reduce swelling, but it should always be used under a physician's supervision. The use of the custom-made elastic sleeve is an essential part of the management.

Brush, B. E.; Wylie, J. H.; Beninson, J.; Block, M. A., and Heldt, T. J.: The treatment of postmastectomy lymphedema. A. M. A. Arch. Surg. 77:561-567, Oct., 1958.

Prognosis in Prostatic Cancer

The outlook in cancer depends on the site and distribution of the disease and on its response to surgery and radiation. Other prognostic aids include early diagnosis, age of the patient and activity of the tumor. All these factors enter into the prognosis of prostatic cancer. Prostatic tumors vary so much in malignancy that the effect of any particular method of treatment and its influence on the prognosis require careful analysis. The higher incidence of latent tumors in postmortem material than of clinically manifest tumors in life supports the idea that neoplastic activity ranges widely between the inert subclinical focus and the fulminating metastatic disease. Cancer of the prostate in elderly patients is often relatively chronic and has a lesser tendency toward secondary dissemination. The choice of treatment generally lies between surgery and endocrine control, radiotherapy having little application due to the insensitivity

of most prostatic cancers. Palliative resection is important for the relief of urinary obstruction. Radical surgery with a view to extirpating the disease has limitations. Few prostatic tumors are detected at a stage when total removal is possible. All these facts are strong indications for allowing some patients, particularly the elderly, to continue to harbor their prostatic tumors. Most prostatic cancers are detected only after the disease has become inoperable. And it is then important to assess the likely effect of hormones. Approximately 80 per cent of cases respond initially to estrogen therapy or castration. The majority of untreated patients die within three years of diagnosis. Nearly 50 per cent of patients receiving estrogen therapy survive five years. The phosphorylated estrogens recently recommended were not found to be superior to the older products. Adrenalectomy and inactivation of the pituitary may be of value in the later course of the disease. The outlook in prostatic cancer is determined to a greater extent by endocrine sensitivity than by histological grading or any other factor which can be measured in the laboratory.

Anon.: Prognosis in prostatic cancer. Brit. M. J. 1:1395-1396, May 30, 1959.

Management of Inoperable Cancer

Patients with inoperable cancer and their families are becoming aware of recent advances in cancer management and are reluctant to accept the verdict that nothing more can be done. The author makes a plea for more careful recording of the description of the tumor in an inoperable patient by the surgeon who sees it, so that the radiologist, the family doctor and the possible second surgeon may treat the patient effectively. Some patients with uncertain diagnoses are operated upon without adequate preliminary studies. If the primary lesion is of borderline resectability, the surgeon must know in advance whether metastases are present or absent. Previously obtained roentgenograms of the chest, spine, skull, pelvis and proximal long bones are often of great value. If leukemia or lymphoma are factors, preoperative hematologic studies are essential. Frozen sections should be used more frequently—the usefulness of hormone therapy, chemotherapy and radioisotopes depends to a considerable degree upon the histologic type of tumor. Along with the pathologist, the radiotherapist may well be present at the operation to see the deep-seated lesions he will be treating later. Certain palliative measures may be prepared for at the operation in which a nonresectable tumor is found. Tubes may be appropriately placed for immediate postoperative instillation of colloidal radioisotopes into a body cavity or into the substance of the tumor.

Andrews, G. A.: Operations revealing incurable cancer. Surg., Gynec. & Obst. 107:787-788, Dec., 1958.

New Teaching Film on Tissue Section Preparation

A new teaching film, "Some Techniques of Tissue Section Preparation in the Pathology Laboratory," in color and 29 minutes long, has been produced by the National Committee for Careers in Medical Technology. This is for use in courses of instruction given to histotechnologists, who are responsible for preparing sections for microscope examination by the pathologist. The film depicts commonly made errors, which result in distortions of tissue, and shows how they may be avoided. The film was shown for the first time at the Annual Meeting of the American Society of Clinical Pathologists and the College of American Pathologists in Chicago last September. The film is for use in any one of the 706 AMA-Approved Schools of Medical Technology. For those interested a preview print may be obtained from the National Committee for Careers in Medical Technology, 1785 Massachusetts Avenue, N. W., Washington 6, D. C.

Role of the Internist in Cancer

Samuel G. Taylor, III, M.D.

With his knowledge in the fields of diagnosis, hematology, endocrinology, and cardiac, respiratory, gastroenterologic and neurologic physiology, the internist's contribution to the total care of the cancer patient is assuming ever increasing importance. It is paradoxical that, despite this fact, the number of applications for research and service grants in cancer which come from departments of medicine is still insignificant compared with those from departments of surgery, pathology and radiology.

Actually, the internist's responsibilities lie in all phases of cancer from the primary diagnosis to the terminal care of the patient.

The primary role of the internist is to use all the available techniques for the early detection of cancer. He should not only know the newer techniques for this detection but also practice them. Yet, in many localities internists have left the responsibility for such simple office techniques as cervical and vaginal cytologic examination to the gynecologist. A look at the larynx by indirect laryngoscopy generally can be performed in an internist's office. And with the aid of the disposable enema kit there is no excuse for avoiding the proctoscope. The guaiac test for occult blood can be done so simply and easily it is a mystery it is not part of every examination. The female breast is not just an organ to push aside in order to better examine the heart or lungs. Adequate time must be spent on these appendages if early unsuspected lesions are to be diagnosed.

The internist is the only physician who can schedule his time so he can obtain a really complete history and do a really complete examination. Such an examination cannot be expected of a busy general practitioner who sees a patient every 10 minutes or a surgeon whose office time is taken up with postoperative follow-ups or referrals for specific surgery. The American Cancer Society's slogan, "Every doctor's office a cancer detection clinic," cannot be realized in large volume practice but can be in the disciplined office of the internist.

The second role of the internist is that of making a decision for therapy when cancer is discovered or suspected. For this decision to be intelligent and of value to the patient he must know the natural history of the disease and the end results, morbidity and mortality of various surgical or radiological techniques. Most important of all he must know the skill of the surgeons and radiotherapists in his community so that he may offer his patients the best possible treatment.

The internist's active participation in the patient's immediate postoperative care frequently reduces morbidity and occasionally prevents a mortality.

Postoperative follow-up of the patient is the responsibility of the internist as well as the surgeon interested in his end-result statistics. For the follow-up to be profitable the internist must be cognizant of the natural history of the disease and the usual sites of recurrences so that he may institute measures to protect the patient from crippling disability as long as possible. The early discovery of lytic metastases in weight-bearing bone and their prompt treatment may prevent debilitating sequelae.

Although most complications of disseminated cancer are caused by direct involvement of specific organ systems, certain syndromes, not directly related to tumor infiltration, occasionally occur. These include hypercalcemia not related to osseous metastases that occasionally occurs in bronchogenic carcinoma and hypernephroma, hypoglycemia in carcinoma of the liver and retroperitoneal sar-

Director, Section of Oncology, Department of Medicine, Presbyterian-St. Luke's Hospital, Chicago, Ill.

coma, degeneration that may occur in any metastatic cancer and occasionally polycythemia. These are all complications best recognized and managed on a medical service.

Aside from the malignant lymphomas and tumors influenced by endocrine alterations, very limited success is obtained from systemic therapy in disseminated cancer, yet functional impairment of specific organ systems produced by metastatic involvement can frequently be alleviated by an imaginative, intelligent internist. The complete investigation of the hematopoietic system not infrequently yields possibilities for more definitive therapy than simply replacing blood for anemia (i.e., hemolytic anemia, unsuspected blood loss, malabsorption). Impairment of the respiratory system from the encroachment of the tumor or accumulation of intracavitary fluid may be the sole causative factor of disability. By selecting proper radiation, surgery or chemotherapy, rehabilitation can frequently be accomplished.

By accurately diagnosing the cause of pain the internist can frequently select the proper neurosurgical, radiotherapeutic, orthopedic or other procedures that will give satisfactory palliation, thus avoiding the distressing complication of narcotic addiction. Addiction is carefully avoided in other chronic diseases even though pain may be more distressing than when caused by cancer. Yet the common, hopeless attitude, not only of the attending physician but of the cancer patient and his relatives, too frequently allows addiction to occur unnecessarily.

Corticosteroids are of great value in pain palliation, improvement of the airway in respiratory obstruction, control of hypercalcemia and of symptoms of cerebral metastases, and may improve the patient's appetite and relieve certain areas in which obstructive edema has occurred. In certain instances these drugs produce actual tumor regression. The internist is an essential member of a team in the management of replacement therapy of hypophysectomized or adrenalectomized patients, but his usefulness is greatly enhanced if he has full knowledge of the natural course of the underlying malignant disease. He is much better equipped to manage a patient on pharmacological doses of corticosteroids and the sex steroids than are those physicians who do not have the basic knowledge of all the pharmacologic actions of these drugs.

Although chemotherapy is in its infancy, programs for screening the myriad of new compounds, which are and will be available, should be in the hands of well qualified internists rather than the surgeon or the radiotherapist who has had to take up this program by default.

In the various stages of cancer many different specialists are called upon to give therapy. A common result is that there are many doctors on a case but no one to manage the total patient. The internist can best fill this role and thereby prevent the patient from feeling that no one is specifically and personally interested.

In the most recent pamphlet on the "Essentials of Approved Residency," no mention is made of a training program in oncology in the medical residency program. Contributions in the field of cancer in departments of medicine will undoubtedly be of greater and greater value if all phases of the disease are adequately emphasized in the training program for medical residency.

It is essential that everything possible should be done to diagnose the maximum number of cases in the earliest stage of the disease [breast cancer] and to carry out the appropriate treatment immediately. It is necessary, therefore, to educate women regarding the warning symptoms of breast cancer and the good results which are achieved by early treatment of the disease.

Raven, R. W.: Malignant tumours of the breast. In *Raven, R. W., Ed.: Cancer, vol. 4. London. Butterworth & Co., Ltd. 1958; pp. 224-245; p. 225.*

LUNG CANCER PREVENTION AND THE PHYSICIAN

Lung Cancer: Foremost Cancer Problem

Physicians in general are well aware of the recent steep rise in the incidence of lung cancer and the emergence of this disease as the leading cause of death from cancer among men (32,000 in U.S. in 1959). They are cognizant also of the etiologic relationship which has been found to exist between cigarette smoking and lung cancer. What may not be fully appreciated, however, is that *we now have at hand the means of controlling a major cancer problem in this country.*

A "Breakthrough"—Lung Cancer Preventable!

It has been estimated that 75 per cent or more of all lung cancer cases could be prevented if the knowledge now available about this disease was fully exploited. The uncovering of this information represents a "breakthrough" in cancer control. It was so described by Dr. Howard C. Taylor, Jr., Chairman of the American Cancer Society's Committee on Tobacco and Cancer, in an address to the Society's Board of Directors in June, 1959. At that time, the Board passed a resolution calling for a more intensified educational program on smoking and lung cancer for both physicians and the general public. It was recommended that particular emphasis be placed on bringing the facts on smoking and lung cancer to the attention of teen-agers before their smoking habits are formed.

American Cancer Society Spearheads Communities' Fight for Youth

A direct result of this action has been the development of the Society's *Teen-age Program on Cigarette Smoking and Lung Cancer.* In preparation for this program, intensive research on the smoking practices of teen-agers was carried out over a period of 18 months. Informed and experienced authorities and specialists on this subject were consulted. Materials were then developed, based on the findings of these investigations. School educators have provided their counsel and guidance in the method of introducing these materials into the school system. The entire program, from its outset and all during its development, has been worked out under the supervision and with the complete cooperation of members of the medical profession.

This educational attack on lung cancer is long-range in prospectus and will encounter difficulties and obstacles. Its effectiveness will depend on the support of the entire community, particularly of parents, teachers and, most of all, physicians. The program will be conducted by the 60 Divisions and 3,000 Units of the American Cancer Society which, through experience and structural organization, are eminently qualified to conduct this type of health education program. It is desirable that this be a voluntary, noncoercive effort which involves both the public and the medical profession in a joint educational project. It must be conducted skillfully and persistently on a continuing basis. The American Cancer Society, with its lay and professional membership, located in every community throughout the United States, has this capability.

Physicians in Control

Physicians will have the opportunity to participate in the program in a variety of ways. Some will be asked to review program materials as members of their county medical societies; others will become members of the American Cancer Society's local committees on smoking and health; many physicians will be advising and guiding parent-teacher associations, youth groups and other public service groups concerned with the problem. There will be a need for physicians as speakers at adult service club meetings, parent-teacher assemblies, student groups, etc. Undoubtedly, there will be many other ways in which physicians can contribute actively to this program in each community. Not the least important is the physician's daily office contact with patients of all ages which gives him special opportunity in this health education endeavor.

As citizens, parents and physicians, the members of the medical profession have the heaviest responsibility as well as the most challenging opportunity to protect the nation's youth from eventual lung cancer—a preventable disease. Their cooperation and participation in this preventive medicine activity is earnestly solicited.

Additional information on this program may be obtained from the local Units of the American Cancer Society.

AMERICAN CANCER SOCIETY

This article has been reprinted from a brochure distributed at the ACS professional exhibit shown at the June 1960 meeting of the American Medical Association.

Radiologic and Cytologic Screening for Lung Cancer; Preliminary Report

Dean F. Davies, M.D., Ph.D.

This report is about detection of asymptomatic lung cancer by periodic radiologic and cytologic screening. The idea for this study was conceived by the members of the American Cancer Society's Lung Cancer Advisory Committee in 1955 and 1956 and was finally activated in June, 1958.

Planning is carried out by a Coordinating Committee consisting of representatives from a Statistics Center, a Radiology Center, four Cytology Centers; and six Veterans Administration domiciliary units as the Screening Centers.

This is a pilot study which was not designed to be definitive. We are really trying to find out on a relatively small scale (about 11,000 men) what the indications are for a larger study of the value of mass screening of a nonpatient population group by cytologic and radiologic means. The study is not designed to examine the value of screening in terms of five-year survival rates. However, if, for example, 90 per cent of unsuspected cases of lung cancer turned up are resectable, semiannual screening would certainly deserve further consideration. On the other hand, if only 5 to 10 per cent of the new cases discovered are resectable, then the value of the screening would not be too great, at least until improved methods of therapy are found.

The Veterans domiciliary unit is an ideal group to examine for lung cancer. In the first place, it consists almost entirely of men, only 1.7 per cent being women. In the second place, as seen in Figure 1, the age distribution of the members of this study closely resembles the age distribution of lung cancer mortalities in the general population. The age distribution of the adult population of the United States, it can be seen, is quite dissimilar.

Another characteristic of this group in making it ideal for finding lung cancer is their smoking habits. In comparison with the smoking habits of the U.S. population as a whole, 93.5 per cent of these men either have smoked or do smoke as compared with 77 per cent of the U.S. population in 1955. Also 23 per cent more of them are currently regular cigarette smokers than in the general population. All of these features add up to make this a high risk group.

After an initial history form is filled out, each member of the domiciliary unit is screened every six months. A stereoscopic pair of 14 x 17 radiographs are taken. At the same time sputum is collected, either spontaneously produced or aided by the

Abstracted from paper, "Problems in Methodology in Radiologic and Cytologic Screening for Diagnosis of Lung Cancer; Preliminary Report from ACS-VA Cooperative Study" presented before the 19th VA-Armed Forces Conference on the Chemotherapy of Tuberculosis, February 10, 1960, Cincinnati, Ohio.

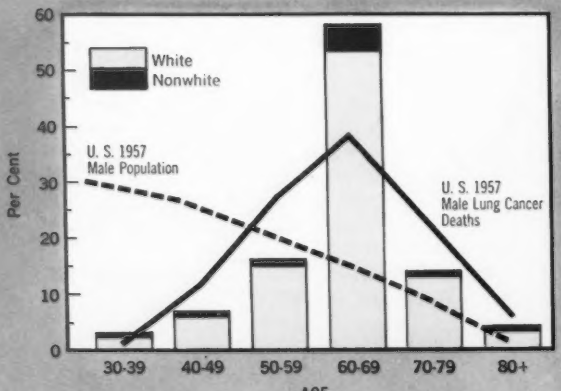


FIGURE 1—*(Left)*

Age distribution of 8,523 veterans in six domiciliary establishments (ACS-VA Lung Cancer Screening Study).

Note: Population includes 91.8% white and 98.3% male nonhospitalized subjects. More than 94% of population are over 45 years of age.

FIGURE 2—*(Right)*

"Expected" and "suspect" lung cancer incidence (ACS-VA Lung Cancer Screening Study).

use of a machine delivering large volumes of an aerosol. This sputagenic machine was invented and developed specifically for this study. The films are read (but not stereoscopically) by the local radiologists, and the sputum specimens are smeared by technicians. The x rays are mailed to the Study's Radiology Center and the slides are mailed to its four Cytology Centers in rotation. Suspects are followed up by physicians at the screening center until satisfactory explanation of x-ray or cytologic abnormality is found. Of course the history form and subsequent symptom supplements may in retrospect reveal how to further narrow down a high risk group.

As might be expected, the radiologists are not always satisfied with the excellence of the films, nor the cytologists with the smears. The technical problems in x-ray screening have been more rapidly overcome than those of cytologic screening. It is clear, however, that the latter method is practicable.

The agreement between radiologists on dual reading of films is lowest (19 per cent) for the "suspect neoplasm" category and highest (66.7 per cent) for the negative film. When suspicions of any significant pulmonary abnormalities—neoplastic and other—are considered together, the per cent agreement between radiologists more than doubles from 19 to 42 per cent of all films so classified by either reader.

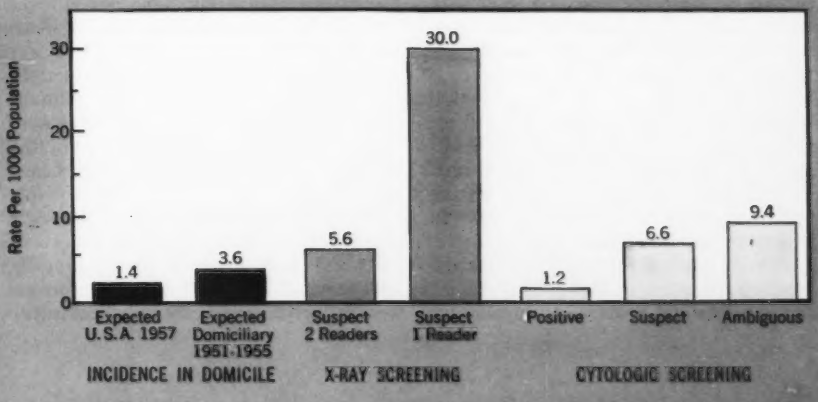
One of the problems that plagued us in the design of the study was whether the size of the population would be adequate to detect enough lung cancer cases to give a reliable cue for expansion or curtailment of research. Figure 2 shows "expected" and "suspected" lung cancer rates per 1000. On the basis of United States lung cancer mortality figures for men of this age distribution in 1957, 1.4 cases per 1000 per year would be expected. Based on estimates from the experience of the VA domiciliary establishments from 1951 through 1955, the rate expected would be about 3.6 per 1000 per year, although this is a less reliable figure.

Where both radiologists agree on x-ray readings, the lung cancer suspects are being found at the rate of 5.6 per 1000. If only one radiologist's classification is accepted to make the case suspect, 30.0 suspects per 1000 are being discovered.

By comparison, cases read as "positive" by cytologists are being discovered at the rate of about 1.2 per 1000, "suspects" 6.6 per 1000 and the designation "ambiguous cells" at a rate of 9.4 per 1000.

The latter term indicates an abnormality with possible prognostic significance not necessarily suspected of having cancer. We are not presently prepared to report on the number of confirmed lung cancer cases picked up by these screening methods.

In summary, some of the details and problems involved in the ACS-VA Cooperative Pilot Study on Evaluation of Radiologic and Cytologic Screening of a Population for Early Diagnosis of Lung Cancer have been discussed. The feasibility of the method of cytologic screening has been demonstrated, but its ultimate value has not been evaluated sufficiently to draw conclusions. Similarly, the ultimate value of periodic x ray as a practical tool for screening for lung cancer is not established.



A Medical Letter Statement on Smoking and Lung Cancer

[The following statement is reprinted from *The Medical Letter on Drugs and Therapeutics*, 2:1-2, Jan. 8, 1960.]

Dr. John H. Talbott, Editor of the A.M.A. *Journal*, has advised physicians (*J.A.M.A.*, Dec. 12, 1959) to wait for "definitive studies" before making up their minds about the causal connection between smoking and lung cancer. In the opinion of *Medical Letter* consultants, physicians should not wait for more studies before warning patients that smoking does increase the risk of lung cancer.

Dr. Talbott's signed editorial in the *Journal* questions the validity of a statement by Dr. Leroy E. Burney, Surgeon General of the Public Health Service, which appeared in the *Journal* two weeks earlier. Dr. Burney, after reviewing the evidence, concluded that smoking is "the principal etiological factor in the increased incidence of lung cancer." But according to Dr. Talbott, "a number of authorities who have examined the same evidence cited by Dr. Burney do not agree with his conclusions." If physicians were to demand unanimous agreement among authorities for medical or public health decisions, they would rarely make a diagnosis, prescribe a drug, or undertake a public health project.

The preponderance of evidence incriminating smoking has been such as to convince eminent epidemiologists, pathologists, clinicians and cancer investigators, as well as the American Cancer Society, the National Cancer Institute, the American Public Health Association, the British Ministry of Health, the British Medical Research Council, and the State Medical Research Council of Sweden. In fact, the probability of a connection between smoking and lung cancer is now so great that for practical purposes in advising his patients, the practicing physician would do well to regard it as proved.

The Refutation—Dr. Burney's report provides statistical, pathological, chemical and experimental evidence to support his conclusions. In questioning these conclusions, Dr. Talbott states that studies on smoking and lung cancer "do not explain why, even when smoking patterns are the same, case rates are higher among men than among women, and among urban than among rural populations." But as Dr. Burney states, there may be a "true sex difference in susceptibility . . . to lung cancer."

There is no reason why a sex difference should be more remarkable in the mortality rate for lung cancer than, for example, stomach cancer (which is far more frequent in men than in women), or for pulmonary tuberculosis. The considerably higher mortality rate for pulmonary tuberculosis in females than in males does not negate the significance of the tubercle bacillus in the etiology of pulmonary tuberculosis. Aside from specific sex differences in susceptibility, a part of the disparity between male and female lung cancer mortality can probably be accounted for by the fact that on the average, men have been smoking for longer periods than women (Haenszel, W., et al: *Public Health Monograph*, No. 45, 1956).

As for differences between rural and urban areas, "the lung cancer death rate was found to be somewhat higher in cities than in rural areas. . . . In all areas, the lung cancer death rate was very low among men who never smoked regularly and high among regular cigarette smokers." [Hammond, E. C.: *Am. Scientist*, *46*:331, 1958]. This finding simply supports the hypothesis that air pollution is another important cause of lung cancer.

Dr. Talbott urges that until "definitive studies are forthcoming" the physician should watch the situation closely and advise his patients on the basis of his own appraisal of the facts. Aside from the difficulty a busy practitioner has in keeping sufficiently informed of the facts to make a scientific judgment, the question arises

as to what is a "definitive study." And how much additional evidence is necessary to incriminate smoking as a cause of lung cancer before personal and public health measures are to be advocated? In 1849, Dr. John Snow showed a connection between cholera and the drinking of polluted water. Thirty-four years later Koch demonstrated the presence of cholera vibrio as the responsible organism. Should steps to eliminate water pollution have waited for Koch's demonstration? Obviously not, and the parallel with cigarette-smoking seems clear.

There are many gaps in our knowledge of the etiology and pathogenesis of lung cancer. But highly convincing studies are at hand to support the conclusion of Dr. Burney and others that smoking, particularly of cigarettes, is an important etiologic factor in the increased incidence of lung cancer; that "stopping cigarette smoking even after long exposure is beneficial"; and that "the nonsmoker has a lower incidence of lung cancer than the smoker in all controlled studies, whether analyzed in terms of rural areas, urban regions, industrial occupations, or sex." [Burney, L. E.: *J.A.M.A.*, *171*:1829, Nov. 28, 1959].

Suggested Reading

TREATMENT OF CANCER AND ALLIED DISEASES, 2nd ed. Edited by GEORGE T. PACK, M.D., and IRVING M. ARIEL, M.D. New York. Paul B. Hoeber, Inc. 1958. Vol. I—646 pages, $22.50; Vol. II—316 pages, $15.00; Vol. III—781 pages, $30.00.

The first edition of this standard collective review of the treatment of cancer was issued in 1940 in two volumes. This second edition has been expanded into nine volumes of which the first three are now available. In Vol. I the principles of treatment are discussed by a group of fifty-five experts in their special fields. The first section, on organization, contains a chapter on prevention of cancer by Hueper and another on cancer detection facilities by Cameron. Similarly qualified authorities present general discussions of diagnosis and pathology, surgery, irradiation, chemotherapy, hormone therapy and reporting of end results. The remaining volumes are devoted to specific forms of cancer classified by site—Vol. II, nervous system; Vol. III, head and neck; etc. The completed nine-volume set will constitute a veritable encyclopedia of oncologic knowledge with special emphasis on treatment—a source book which no physician with cancer contacts can do without.

MIND IF I SMOKE? By HAROLD SHRYOCK, M.D. Portland, Oregon. Pacific Press Publishing Association. 1959. 138 pages. $2.50, cloth-bound, $.50, paper-bound.

The author has succeeded in condensing all the important contributions to the knowledge of the hazards of smoking into a few pages. Lung cancer, cardiovascular damage and injury to other tissues are detailed in language suitable for the physician and yet simple enough for the intelligent lay reader. The paper-bound edition might well be available in quantity in every physician's office to hand to the patient requesting information in this field.

The Simplest Test for Making the Diagnosis in Bronchogenic Carcinoma

George C. Adie, M.D.

The purpose of this article is to re-emphasize what is already common knowledge. The examination of the sputum for neoplastic cells is a simple and effective procedure. It is frequently overlooked in a desire to proceed directly to a more complicated and often less rewarding study.

The frequency of bronchogenic carcinoma is high and on the increase, while the survival time is not being improved. This suggests, of course, that greater efforts should be made to detect the disease in the early stages. More frequent use of chest x-ray examination is essential; when any suspicious lesion is found, every diagnostic aid should be utilized to reveal its true nature.

Atelectasis, pneumonitis and round lesions should never be regarded lightly.

Bronchoscopy permits direct visualization, tissue biopsy and collection of bronchial washings. This procedure is especially useful in lesions of the main bronchi and their major subdivisions. It may give evidence as to the gross extent of the lesion, the degree of fixation of the bronchus and any displacement of hilar structures. When the lesion is located peripherally, useful information is not often obtained by this method. By bronchoscopy alone, it is reported by various writers, the diagnosis can be established in 35 to 55 per cent of cases. It is also commonly reported that cytologic studies of bronchial washings show abnormal cells in 30 to 70 per cent of cases. When the percentage of positive findings is high, the incidence of proximal lesions tends to increase the positivity rate. In peripheral lesions, the finding of positive cells in washings is less frequent.

The removal of scalene nodes for diagnostic purposes is not too fruitful, certainly in the early cases; if mestastases to the nodes have occurred, spread of the disease has taken place and an unfavorable prognosis is indicated.

The one examination not requiring bronchoscopy, or any operative procedure, is the study of the sputum for abnormal cells. Any lesion of the bronchial tree, large or small, peripheral or central, is constantly shedding cells and at one time or another they appear in the sputum. One specimen may not reveal exfoliated cells; therefore more than one should be collected because the chance of finding positive cells increases with the number of specimens.

The patient should be provided with a wide-mouth bottle in which there is a fixative solution composed of formalin, ether and acetic acid. He should be instructed to expectorate directly into the bottle. The entire production of sputum should be collected for 24 hours. Three such specimens are advisable.

Dr. William C. Schraft, Director of Pathology, assisted by Dr. Silvestre Lingad, the Pathology Resident, in the progress of reviewing the findings from cytologic studies in bronchogenic carcinoma at the New Rochelle Hospital for the past eight years, has produced the following data from the records investigated. Every case admitted was not subjected to complete laboratory studies nor has the entire group of some 200 cases been analyzed.

From tissue obtained in 84 bronchoscopic examinations 36 positive diagnoses could be made, which represents an accuracy of 43 per cent. From the bronchial washings obtained in these 84 cases, 41 showed malignant cells for an accuracy of 49 per cent. There were 65 sputum examinations; of these, 27 represented one or two specimens and most were felt to be improperly collected. In 38 cases, the remainder of the 65, at least three specimens were submitted and collected according to laboratory specifications. In this group

From New Rochelle Hospital, New Rochelle, New York.

there were 33 positive diagnoses for an accuracy of 87 per cent. In the entire group of 65 sputum specimens examined there was a diagnostic accuracy of 51 per cent.

While the number of cases examined is not large there seems to be sufficient evidence already established in this group that the effectiveness of sputum studies for cytology should again be emphasized.

When the x-ray findings indicate a peripheral lesion suggestive of carcinoma and the sputum examination is found to be positive for neoplastic cells, it is possible that bronchoscopy might be obviated.

If bronchoscopy is indicated, the sputum specimens can be collected while the patient is awaiting admission to the hospital. Larger and more central lesions should always be subjected to bronchoscopy because direct or indirect evidence thus obtained will be of great value to the surgeon at the time of resection.

Fourth National Cancer Conference

Under the co-sponsorship of the American Cancer Society and the National Cancer Institute, the Fourth National Cancer Conference will be held September 13, 14 and 15, 1960, at the University of Minnesota in Minneapolis. The theme of the three-day meeting will be "Changing Concepts Concerning Cancer." All members of the medical and dental professions, students, and those working in allied sciences are invited.

All inquiries should be addressed to: Coordinator, Fourth National Cancer Conference, American Cancer Society, Inc., 521 West 57th Street, New York 19, N. Y.

The Cigaret Smoker and Lung Cancer

Morton L. Levin, M.D.

Q: *Dr. Levin, last October,* Modern Medicine *published an interview with Dr. Clarence Cook Little, scientific director to the Tobacco Industry Research Committee, concerning the relationship of cigaret smoking and lung cancer. He was critical of the various studies and reports to date that suggest a cause-and-effect relationship of smoking to lung cancer, and he insisted that scientific conclusions cannot be made at this time. What is your opinion on this issue? Is there a direct cause-and-effect relationship?*

A: The consensus is that some type of cause-and-effect relationship is the most reasonable interpretation of the known facts. Other interpretations are largely speculative. The term "cause" has many legitimate meanings. Like other known environmental causes of cancer in man, tobacco tar seems to behave as an effective, but not a necessary "specific" or "sufficient" cause. The etiology of cancer is exceedingly complex and its mechanism obscure. This is as true of tobacco as of other carcinogenic materials. This does not prevent us from utilizing the practical implications of the carcinogenic effect of such agents as chromate compounds, trivalent arsenic, certain aromatic amines, or ionizing radiation.

Q: *You do not agree with Dr. Little, then, that the statistical study reported last year by Drs. Hammond and Horn is inconclusive as to cause-and-effect relationship?*

A: No. The question, for one thing, is misleading because it suggests that this is the only type of evidence supporting a cause-and-effect relationship, which is not true. If it were the only type of evidence that one had to consider, it would be highly suggestive, though not conclusive. But when you take it in conjunction with all the other evidence, then I would say the relationship is established almost as well as it could be without direct experiments on human beings.

Reprinted from Modern Medicine.

Q: *Perhaps it would be helpful here to identify your interest in this problem.*

A: I have just resigned from the New York State Department of Health, where I was assistant commissioner for Medical Services, closely concerned with research in cancer. I have accepted an appointment as professor of Cancer Epidemiology at Roswell Park Memorial Institute, Buffalo, N. Y., under a grant from the American Cancer Society.

Q: *What is the background of your work in the epidemiology of cancer?*

A: After earning my medical degree at the University of Maryland, with internship at Sinai Hospital, Baltimore, I became assistant physician at Johns Hopkins Hospital and was a fellow in the Johns Hopkins School of Hygiene and Public Health. Later, I was an instructor in the Department of Epidemiology. Dr. Thomas Parran was then New York State Commissioner of Health and invited me to the staff of Roswell Park Memorial Institute to combine the methods of epidemiology with the cancer problem.

Q: *When was that?*

A: In 1939. We began to collect cases at Roswell Park Memorial Institute to analyze for clues concerning characteristics of cancer patients. I thought then that study of the smoking habits of patients before diagnostic work-up would provide a clear-cut answer to whether the use of tobacco was associated with any increased cancer risk. At that time, I was far from convinced that there was any association, except that between pipe smoking and lip cancer.

Q: *What did your study reveal concerning lung cancer?*

A: We were surprised to find a strong correlation between smoking and lung cancer. Ours was a retrospective, case control study which compared the smoking his-

tory of a large number of patients with all kinds of diseases, half of whom had no tumors of any type, with persons who had various forms of cancer. The most striking thing was that the proportion of cigaret smokers with lung cancer was considerably higher than with any other disease.

Q: *Have there been any other findings?*
A: Cigaret smoking was also significantly associated with laryngeal cancer. The proportion of pipe smokers who had lip cancer was also considerably higher than of nonsmokers. This has been known for a long time, though not so thoroughly documented as one would wish. Our study was published in the *Journal of the American Medical Association* in May 1950. That issue also contained the report by Wynder and Graham indicating substantially the same findings. I think these papers stimulated a good deal of the intensive investigation that has followed, because they convinced a great many people that the subject was worth looking into.

Q: *What has happened since the papers were published?*
A: There have been 28 studies of the retrospective type, in which the histories, habits, and characteristics of persons with known disease are compared with some other group with no disease or another disease. These studies have been done in a number of countries and on various types of clinical and control cases. All have shown about the same results. In addition, there have been three studies of the prospective type, in which a large group of persons with apparently no disease have been studied. Their smoking histories and other characteristics are recorded and then they are followed periodically for whatever disease may develop. Such studies have been made by Drs. E. Cuyler Hammond and Daniel Horn of the American Cancer Society, by Drs. A. Bradford Hill and Richard Doll in England, using the physician population, and, the most extensive, by Dr. Harold Dorn of about 200,000 American war veterans.

Q: *Is there evidence aside from the retrospective and prospective human studies you have mentioned that links cigaret smoking with lung cancer?*
A: Yes. There is considerable evidence from the experimental laboratory.

Q: *Will you describe some of that work?*
A: The early observations of Kennaway on chemical carcinogenesis showed that pyrolysis of various organic materials, such as coal, skin, hair, yeast, petroleum, and cholesterol, produces carcinogenic tars. So it would not be surprising if an organic material such as tobacco does the same thing. The British have done much work in this field. At least eight chemicals that were previously known to be carcinogenic in animals have now been identified as being constituents of cigaret tars.

Q: *Those chemicals are in the tar of cigaret smoke?*
A: Yes, in the smoke produced by simulating the conditions of ordinary smoking. The main-stream smoke obtained is a very complex substance in which about 150 elements and compounds have been identified, including cancer-producing chemicals. This is not direct proof that smoke actually produces cancer in human beings but is sufficiently suggestive to justify study of human beings exposed to this substance to see whether they do have a higher cancer incidence than those persons who have not been exposed.

Q: *Tobacco tar has produced cancer when painted on the skins of animals, but this is not the same type of exposure as with smoking.*
A: No, it's not. It does establish the fact that tobacco tar is carcinogenic for some animal tissues. One of the established principles in experimental cancer research is that there is no necessary species or tissue correspondence. In other words, there is no reason to suppose that a chemical that produces a particular kind of cancer in one species or tissue will do it in another. Until recently, chromium compounds and

arsenic would produce no tumor in animals, although they are carcinogenic for man. Tumors have now been induced in animal tissue with chromium compounds, though not of the lungs, but arsenic still has no demonstrable carcinogenic effect in animals.

Q: *Are there other types of experimental carcinogenic activity, aside from skin painting, that implicate tobacco tar?*

A: Hyperplasia, metaplasia, and other changes in the bronchial epithelium of dogs and mice have been produced, but not full-blown tumors. The changes could be considered to be on the road to neoplasia. It also has been shown by autopsy examination of the lungs of persons whose smoking histories were known that similar cell changes in the bronchi correlate with smoking.

Q: *Do you consider the changes to be precancerous?*

A: There is a lot of argument as to whether the changes are precancerous, but there is agreement that they are pathologic. An interesting finding is that such pathologic changes are as frequent in the tracheal epithelium of smokers as in the bronchial epithelium, although bronchogenic carcinoma is much more frequent than tracheal. This may be due to differing tissue susceptibility, to varying intensity of exposure to tobacco tar particles, or to other inspired carcinogenic agents. The reason is at present speculative. However, we are familiar with the fact that the same agent may produce different effects in different tissues of the same species. What we are left with is: (a) Tobacco contains known animal carcinogens and (b) pulmonary epithelia in smokers show more pathologic changes than those of nonsmokers.

Q: *What do these facts imply?*

A: The question then is, do these people have a different experience with respect to the incidence of or mortality from lung cancer than the rest of the population? That they do have such a different experience constituted the first impressive findings, both in retrospective and prospective studies. There is the further observation that, concomitant with the increased use of cigarets, there has occurred a rather striking increase in mortality from lung cancer in most Western countries. No other important cause of death has increased to the same extent. This of course is an indirect tie, but, coupled with all the other data, it becomes significant. If the increased use of a suspected substance did not alter the mortality statistics, we would wonder why this had not occurred. The fact that it has occurred is confirmatory evidence. There also is a peculiar age distribution in lung cancer that differs from most other forms of cancer. The incidence of most forms of cancer increases steadily with age, and, although the rate of increase may slacken off, it seldom reverses. With lung cancer, the curve reverses at about age 65 and starts downward. This is particularly notable in males.

Q: *And you blame that on the use of tobacco?*

A: It is consistent with the tobacco hypothesis. Cigaret smoking is least common in people who are now past 65; they formed their smoking habits before cigarets became popular. If they smoke, they are more likely to use pipes or cigars. The change in the use of tobacco over the past 30 years has been most notable with respect to the form of tobacco used. During 1920-55, cigaret consumption in the United States per person over 14 increased about fourfold; the use of other tobacco products decreased about two-thirds.

Q: *Has it not been suggested that cigaret smokers have more of a tendency to inhale than do pipe or cigar smokers?*

A: Yes, a number of studies have shown this. Few pipe and cigar smokers inhale the smoke deeply.

Q: *Statistics on incidence of lung cancer seem to indicate it is a disease that affects men predominantly. What is the explanation for that, in view of the fact that so many women smoke cigarets?*

A: Several studies have shown that women nonsmokers have about the same lung

cancer mortality as male nonsmokers and that women smokers experience higher lung cancer risks than nonsmokers. Most of the studies in the past have been concerned with men, because smoking, particularly heavy smoking, is much more prevalent in males.

Q: *So the sex factor that was thought to prevail in lung cancer now is contradicted?*

A: There is not as much evidence as we would like to have, but studies show that there is less sex difference than we had thought. Of course, we must remember that there are other known etiologic factors in lung cancer, such as environmental exposure in some occupations, that would make the disease more likely to be a male hazard. However, for the same smoking exposure, present evidence shows a higher lung cancer risk among males.

Q: *Isn't air pollution a possible hazard that would affect both sexes alike?*

A: If air pollution were a major factor, the sexes would be more equally exposed than to smoking. However, they would not necessarily respond to the same degree.

Q: *How would you answer the suggestion that cigaret smoking is merely one attribute of people who are going to have lung cancer — that it is more or less a psychologic manifestation of cancer-susceptible people?*

A: That is the constitutional theory. It does not explain many facts. It would not be consistent with any actual increase in the incidence or mortality of lung cancer unless the psychologic or constitutional type had suddenly increased in the human population. It would not correlate with the fact that cigaret smoking is so much more closely tied up with lung cancer incidence than is pipe or cigar smoking, while the latter is associated with cancer of the lip and buccal cavity. Assuming that there is a difference between people who smoke and people who don't, that difference would have to be shown to be as great among persons with lung cancer as the smoking difference and to be a better explanation of cancer than the fact that they were exposed to a substance known to contain cancer-producing chemicals. And what would be the explanation for the decrease in cancer rate among ex-smokers? All of these observations are inconsistent with the constitutional theory as the chief explanation for the lung cancer risk among smokers.

Q: *Of what significance have the various studies been?*

A: For the first time in an important form of human cancer, there is a reasonable prospect of prevention for a majority of cases. This represents a breakthrough in the cancer field, at least theoretically. Obviously, there are strong social and individual barriers to eliminating or modifying this factor. Another significant point is that an important etiologic factor in human disease was discovered primarily by clinical and epidemiologic study. This has been true of other environmental etiologic factors in human cancer. Since most human cancer still is of unknown etiology, there is hope that further study of this type may uncover other environmental factors as yet unknown. On the other hand, the correlation of cigaret smoking and lung cancer has added nothing new to basic knowledge about carcinogenesis. It is completely in conformance with previously known facts about cancer in man and in animals. Production of cancer by a substance resulting from combustion of an organic material at fairly high temperature is exactly what you would expect.

Q: *Dr. Little asserted that the American Cancer Society is crusading and using high-pressure propaganda in an attempt to convince the public that the Society is correct in its interpretation of recent studies as to a cause-and-effect relationship between the smoking of cigarets and lung cancer.*

A: Well, of course I can see how Dr. Little would honestly feel that way. Actually, the Cancer Society approached the whole thing with considerable caution and skepticism. Their first reaction to the clinical case control studies was to point out the possible bias that might be present in such studies. Subsequent experience has shown that whatever bias occurred in the case-

control studies served to minimize rather than to increase the observed association with smoking. The Society proposed a prospective study conducted by its own staff. Only after that showed very much the same results as the retrospective studies were the statisticians for the Cancer Society convinced.

Q: *What did the Society do then?*

A: Before the board of directors of the Cancer Society issued any definite statement, a special study group, in cooperation with the American Heart Association and the U. S. Public Health Service, was asked to review all the evidence. Their report said: "The sum total of scientific evidence establishes beyond reasonable doubt that cigaret smoking is a causative factor in the rapidly increasing incidence of human epidermoid carcinoma of the lung," and they recommended that the findings be applied as a public health measure. The board of directors did not accept that at once. They appointed an ad hoc committee headed by Dr. Howard C. Taylor, Jr. After this committee had reviewed the evidence, the board agreed that the Society should formally support the view that cigaret smoking is an important causal factor in lung cancer. Perhaps Dr. Little's characterization of what they have done as propaganda refers to the dictionary definition of propaganda as the promulgation of a particular point of view because of a special private interest. The special interest of the Society is to advance the prevention and treatment of cancer. Propaganda would be a term even more properly used with reference to the statements made by persons having a private financial interest in the sale of tobacco products.

Q: *Nevertheless, even though the Hammond and Horn study implicated cigaret smoking in coronary heart disease, the American Heart Association has held back for more conclusive evidence.*

A: Although it was not a new observation that there is an association between coronary disease and smoking, I think the Heart Association considered there hadn't been enough investigation of the nature of the relationship and wanted to wait for more evidence, with which I would agree. The increased mortality from ischemic heart disease among cigaret smokers may be more important than the risk of cancer of the lung.

Q: *In the interview with Dr. Little, he said that one group, referring to the American Cancer Society, "insists that present information is conclusive and represents the end of the road." He said ". . . there is great danger if any organization or any group of people attempts to put a limit on the creative thought of others". This attitude, he pointed out, is in contrast to his opinion and that of the tobacco industry that further search must be carried out to establish definitely or disprove a cause-and-effect relationship between the smoking of cigarets and cancer of the lung.*

A: I think the smoking-lung cancer observations have stimulated more research in lung cancer and in the effects of tobacco and also in the epidemiology of cancer than has occurred in the past twenty years. It has opened up many more questions for investigation. However, no one would want to say that the findings of research are not made use of until all of the answers to all of the questions are in, because that would mean you would never use anything.

Q: *What would you suggest a doctor advise a patient who is concerned about the possibility of cancer from cigaret smoking?*

A: Every doctor knows that, in giving advice regarding prevention of disease, we do not usually have available absolute certainty. We have to deal with either high or low probability. The conservative advice would be to point out that smoking cigarets is an important environmental causal factor in the production of lung cancer. Removing it would have preventive effect. Anyone who, after reviewing all the evidence, would say all this can be ignored would be going against the weight of the evidence.

Q: *Dr. Alton Ochsner has observed that usually those doctors who make light of the findings are smokers.*

A: There is something in that. I think there is a natural tendency to be a little defensive about smoking, especially if you try to give it up and then fail. I have noticed this with both doctors and laymen. If a person is concerned and wants to reduce his chances for developing lung cancer, he would be well advised to do one of several things. If he is smoking cigarets, cut it down or cut it out. Perhaps he can switch to a pipe or cigars. Some day, there may be a noncarcinogenic tobacco or a nontobacco, noncarcinogenic cigaret, which of course would solve the problem.

Q: *Do you believe that filters on cigarets are effective protection against the possibility of developing lung cancer?*

A: I don't know of any really good evidence one way or the other. If the filter actually reduces the amount of tar inhaled, this may be equivalent to smoking less. There is no good evidence on which to base an opinion at this time, although studies now under way may add some information when analyzed in a few years.

Q: *You have mentioned the psychologic problems associated with stopping smoking. Is there any way to bolster a smoker's will power or make it easier?*

A: In Sweden, there are medical clinics set up to help people who want to give up smoking. It's a form of habituation which has received relatively little medical attention.

Q: *What therapy do the clinics provide?*

A: One of the things being used is the administration of lobeline, an alkaloid that has a physiologic effect similar to nicotine. In Sweden, placebo studies to determine the effectiveness of lobeline have shown that placebos are just as effective as the alkaloid. I appreciate the psychologic aspects of smoking. I was a heavy smoker for twenty years and I know that giving up the habit of smoking is not easy.

Q: *You recently were in Geneva on a World Health Organization assignment concerned with the epidemiology of cancer, were you not?*

A: The director general of WHO asked a group of us to advise him as to what kind of cancer research might be undertaken by WHO. A number of specific problems were suggested, including some in the epidemiology of cancer. One of the suggestions was that study of the differences in the epidemiology of lung cancer between one country or area and another might be helpful. Other projects suggested were in the epidemiology of cancer of the liver, stomach, cervix, and bladder and of leukemia. There are apparent differences in the mortality from these types of cancer in a number of countries.

Q: *Where do differences exist in regard to lung cancer?*

A: Japan, Norway, and Sweden have rather low lung cancer mortality rates. Cigaret consumption in Japan is about half as much as in the United States, although it is said that the Japanese smoke a great many homemade cigarets which are not included in statistics. Differences in lung cancer mortality in different countries require further study and the establishment of standards on which comparisons can be based.

Q: *Dr. Levin, how would you summarize the present status of the cigaret-lung cancer issue?*

A: Most people who have done work on the problem agree that cigaret smoking is a significant causal factor in a majority of cases of lung cancer. This is the considered judgment of the British Ministry of Health, Medical Research Council of Great Britain, New York State Department of Health, U. S. Public Health Service, and American Cancer Society.

Cancer Orthodoxy

G. W. Taylor, M.D.

A great deal of recent writing on the subject of cancer questions or challenges most of the basic assumptions upon which orthodox methods of management are based. While an unwillingness to accept dogma is a wholesome aspect of the scientific mind, the substitution of a whole new unproved concept may merely serve to confuse the picture without offering any helpful contribution.

These new heresies have many superficial points of similarity with the religious schisms which characterized the Protestant Reformation. The challenge of dogma and rebellion from authority are the common points of departure. It should be remembered, however, that the orthodoxy of cancer ideology is based not upon divine revelation but upon the accumulated observations and clinical experiences of generations of practitioners. Some of the newer promulgations, such as "biologic predeterminism," seem to parallel the doctrine of original sin. Some of the newer heretics seem to bask in a smug certainty of righteousness comparable to the state of grace so eagerly sought by some of the earlier divines.

Unfortunately, some of these newer concepts appear to be wholly sterile and to lead to no fruitful amelioration of management. To sit down with the patient and deplore the whole disease process will not cure cancer, nor even comfort the sufferer. The attitude of mind that accepts predeterminism is close to despair and decries the physician's obligation to endeavor to better the situation.

The pernicious mischief of these heresies is that they are eagerly embraced by the incompetent and ignorant as justification for deviations from approved methods of management. To destroy the physician's faith in his capacity to modify events in behalf of his patient, to deny him the belief that there is a way of salvation sanctioned by authority, is to nullify his social usefulness. Until the heretics can enunciate a formula more constructive than our present orthodoxies, only harm can result from dissemination of their ideas.

Reprinted from Surg., Gynec. & Obst. 107:658, Nov., 1958.

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Heterodoxy in Cancer Therapy

Ian Macdonald, M.D.

Although the editorial by Grantley W. Taylor repeatedly refers to "new heresies" in the plural, he identified (also plurally) only that form of heresy for which I coined the expression "biologic predeterminism" in 1950.[1] This belated, but not unemphatic denunciation of our undistinguished efforts toward a better understanding of the natural history of cancer we regard as the most signal honor which has yet been accorded our particular variety of heterodoxy. For so stentorian a protest from the heart of New England may, perhaps, indicate that such intellectual flummery has made its insidious entry into Boston as an eight-year-old backwash from the frenetic frontier of Southern California, ordinarily regarded by many Bostonians as an academically arid area.

If this conjectural exercise is of any validity, the ire of Dr. Taylor is entirely comprehensible, but offers no contraindication to as vigorous a counterattack as the

From the Department of Surgery, University of Southern California, School of Medicine, Los Angeles, California.

writer can provide, and all the more so from so effective a vantage point as the pages of *CA*.

If the attitudes expressed by Dr. Taylor were correct I would be exposed as an utterly incompetent investigator and a charlatan of sorts, with a distinctly low level of perception to boot. Fortunately, any tangible issues raised are uniformly erroneous, while the intangible and even emotional phrasings speak for a measure of insecurity of the orthodoxian concerning his orthodoxy. I hold no particular affection for the implications of predeterminism in disease, but the evidence is sufficiently convincing as to demand recognition.

In the first paragraph, the key word is "unproved," as applied to predeterminism. From a broad viewpoint, the evidence which was presented in the original articles in 1950[1] and 1951[2] produced a concept which was synoptically expressed as follows: "the balance of power between neoplastic and reactive influences in the host has been established in the preclinical phase of the process, and in a clinical sense this concept may be expressed as that of biological predeterminism."[2] In a restatement of this approach, in 1958, based on further evidence from larger groups of patients with various types of cancer, and viewed in relation to end results of treatment, one of the conclusions was: "the outcome of the preclinical struggle for power, between a developing neoplasm and the enigmatic defensive reactions of the host, is of greater prognostic importance than the time or type of treatment."[4]

The original supporting data were those of duration and dimension of the primary neoplasm, correlated with local spread, or curability, or both, for carcinoma of breast, stomach, colon, uterine cervix and sarcoma of bone. Of these, only for the cervix was there a consistent relationship between duration and curability, but here it was of such critical importance as to emphasize the extreme importance of treatment instituted *one month or less* after the onset of symptoms.

Gastric carcinoma and bone sarcoma, by contrast, were found to have an unfavorable natural history, as indicated by a direct ratio of duration of symptoms to curability, i.e., increasing periods of delay, from onset of symptoms to definitive treatment, were attended by comparable increments both in resectability and curability. For gastric carcinoma, the data were obtained from a series of 6242 patients at the Mayo Clinic, and the more favorable status with increasing periods of delay appeared in the 1951 article[2] in tabular form:

GASTRIC CARCINOMA

Delay interval	Resectabil. %	5-yr. survivors %
0-3 months	35.8	20.8
7-11 months	42.5	23.2
1-2 years	45.0	27.2
3-4 years	53.9	38.5

The biology of mammary carcinoma is much more variegated than any of the preceding neoplasms, as will be outlined in a more suitable frame of reference, below.

In Dr. Taylor's second paragraph, an analogy is drawn between early Protestant sects and our refusal to accept a uniform faith in "early" treatment of cancer, with "rebellion from authority" as a common point of departure. We (the heretics) are advised to heed the orthodoxy based on "accumulated observations and clinical experiences of generations of practitioners." This rhetorical statement epitomizes the perpetuation of error with which the history of medicine is replete. But in this instance a whole body of well-meant propaganda has been built around an oversimplification of a complex problem. Only by an objective study of various forms of cancer were the fallacies and exceptions to the traditional attitudes exposed, and with no helpful spark of "divine revelation." Our earliest approach to the natural history of cancer was not undertaken with any preconceived concepts. It was a realization of the frequent contradictions to the traditionally accepted value of "earliness" in

time and size which prompted me to attempt an evaluation of their real importance, an effort which began in 1946. A search of the literature was singularly unrewarding; it was common for authors to preface their presentation of end results with lamentations over the failure of patients to present themselves for treatment "early" in the disease, but to find a correlation of end results with duration or tumor size was a rarity. Everyone had been genuflecting at the shrine of "early diagnosis," but none of its votaries made any effort to surround the shrine with good, unassailable walls of documentary proof.

Even if I ignore the more contumelious and derisive language, Taylor betrays a sterility of thought by implying that the "heretic" lacks both sensitivity and intelligence when he makes the absurd assumption that one would "sit down with the patient and deplore the whole disease process"! I have never suggested that the true perspective of the curability of cancer should be any part of public education, and I shall suggest the possibility that patients for whose care I am responsible have as firm a belief in their prospect of cure as do those who are cared for by my distinguished critic.

More important, and just as inaccurate, is the statement that "predeterminism is close to despair and decries the physician's obligation to endeavor to better the situation." Let the words Dr. Taylor has not read, or understood, speak for themselves.

> An appreciable fraction of cancers which by clinical standards are late represent biologically dilatory processes susceptible of cure.
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> This sort of evidence is indication for a radical change in the clinician's philosophy of cancer therapy. Rigid ideas of prognosis in terms of duration and dimension should be abandoned in favor of an attempt to evaluate the biological potential of a neoplasm in an individual host. Tangible factors presently available for such an evaluation are admittedly imperfect, but in some forms of cancer the sum of evidence provided in their rate of growth and gross and histologic features constitutes reasonably accurate information.[2]

Those who regard predeterminism as an expression of therapeutic futility must reject entirely the inexorability of natural selection in cancer. Some types of cancer do have a natural history which generally conforms to the traditional doctrine that curability is directly related to the "earliness" of diagnosis, the "immediacy" and the effectiveness of treatment. These are the forms of cancer in which both the degree of space occupation by the primary neoplasm, and the anatomic extent of regional and distant metastasis, is a function of chronologic duration. Such is the natural history of squamous carcinomas of the skin, lip and uterine cervix, which represent a mid-zone in the spectrum of biologic predeterminism.[4]

The futility, or even the unfavorable effects of surgical treatment in some forms of cancer, should not obscure the curative and palliative accomplishments of adequate, meticulous, operative procedures . . . responsible for the major share of present rates of clinical control.[4]

Indicated (in a figure) is an estimated distribution of 100 patients (with breast carcinoma) based on factors inherent in biologic predeterminism (and for which multiple sources of evidence have been shown). Twenty individuals would have a favorable result, usually curative in effect, even with something short of ideal treatment, at any time up to three years after onset. Forty-five to 50 of each 100 have neoplasms of high growth potential and inadequate host-resistance, in whom regional or distant metastasis is established before the primary lesion is clinically apparent. In the remaining 30, there should be the relationship between time, space occupation and metastasis implied in the traditional concept of "early" diagnosis.* *For these 30 women, the extent of their disease is indeed a function of time. It is for this group that not only prompt, but adequate, effective treatment may mean the difference between cure and failure, between life and death.*[3]

The final stone thrown at predeterminism is one I have become expert in dodging; expressed by less caustic critics than Taylor, the pitch is a gentle appeal to reason, i.e., to forsake the "party line" of early diagnosis and early treatment is to confuse the family physician, who will then become entirely pessimistic. Further, it is argued, this concept of variability in the potential of cancer in the individual is too difficult for the average physician to grasp. There are several answers to this, but the most important deserves great emphasis: the truth as it is known, or as it seems to the qualified observer, is the most effective stimulus of interest and the best preventive against apathy for the professional audience. Many thoughtful physicians who had never operated upon a patient with cancer were well aware of the fallacies inherent in the oft-repeated message of "earliness" long before the present crop of "heretics" were being heard. I suggest that the Boston specialist exhibits a pose of superiority toward the family physician which is hardly warranted in the face of his own failure to acquire any vestige of the implication of predeterminism. My own faith in the "average physician" is such that I reject the notion that he acts effectively only when his beliefs are sanctioned by "authority"; his social usefulness will be increased by any challenge to authoritarian concepts which induces new thought, renewed observation and personal efforts at evaluation of old vs. new ideas. Many general practitioners have become keen observers of the natural history of cancer as seen in their own practice, through the stimulation provided by nontraditional ideas; from such reappraisals many of them have come to understand the limited importance of time and space occupation in cancer, to appreciate the significance of the individualization of each patient. With such attitudes becoming more prevalent, usually without benefit of any polysyllabic verbalizations such as predeterminism, there has developed an increasing awareness of the importance of the consultative process toward selection of the most promising therapeutic methods, directed either at cure or palliation. Thus the shrugging off of outworn orthodoxy has resulted in more constructive attitudes, to the benefit of the patient.

As to the incompetent and ignorant who may embrace eagerly our heresies to justify their deviations from "approved methods," I must remind the editorialist that I use the same "approved methods," though in a less historic milieu, but I do not apply any set of rules of "inoperability" to the individual patient. I have a slogan, too, which provides for an occasional patient a chance for cure, or long-term palliation, that he might not have been afforded in areas where the theme of "earliness" is dominant. This slogan points up the insubstantial nature of such academic differences as gave rise to this prolix communication, for I am sure that Grantley Taylor will agree with this item of my faith: "Late Cancer May Also Be Curable."

His prose creates most grievous doubts
Among the medical classes
His heterodoxy is decried
As dangerous for the masses
His major thoughts are classified
Among the noxious gases.
Physicians awake!

(paraphrased from Lawrence Durrell)

From this one may derive an estimated, idealistic or utopian "cure" rate of 55 per cent at five years. This was 10 per cent better than our previous, best estimate, due to a larger sample, 694, of which almost 10 per cent of patients had come to radical mastectomy when the primary lesion was 1.0 cm. or less in diameter; of this group only 40 per cent had microscopic evidence of spread to axillary nodes. Thus, we contributed valid support to the relative value of diagnosis at an early phase, which is more than can be said for those who overemphasize its importance, but rarely take the trouble to determine to what degree the facts fit their slogans.

References

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Example, not Precept

[*Excerpted from* "A Smoker's Letter to His Son," *by Harold Mehling in* Pageant, *February 1960. Dad's dilemma is simple compared to the sorry plight of the nicotine-hooked physician, responsible not only for his own young-uns—"Pop, if you'll stop smoking, I'll never start," but also for advising his patients, adult and adolescent—"Doctor, if it's so harmful, why do you smoke?"*—ED.]

Dear Roddy:

About that proposition you offered your mother and me the other day—the deal about smoking. It deserves a better answer than it got during dinner when you said: "If you'll stop smoking, I'll promise never to start." I'm sorry to say that we have to turn you down. We're ashamed of our decision, but we're going to go right on smoking.

You'd heard something on television about smoking and lung cancer, and you asked a couple of questions. In that direct and simple way of yours, you asked: "Is smoking good for you?" And we said, no, we guessed it wasn't. And so you sprang the trap by asking: "Then why do you smoke?" and we said, well, because it's a habit, we suppose. Here we had a chance to make sure that an eleven-year-old boy—our own son—would never suck all this poison into his body. We could have bought peace of mind in knowing that you were cutting down the chances of suffering and dying from what Arthur Godfrey called "this horrible thing."

We find we don't have the strength to give up our pleasure. Smoking is somewhat intoxicating, and we enjoy it. You see, *we're trapped.* All children whose parents haven't been able to give up smoking might as well understand that and start getting used to it. Their parents are trapped just as surely as if they were addicted to narcotics. All the cancer scares in this world won't stop us now.

You don't believe that we adults are that hooked? But we are! We go to a theater and can't sit through an hour-and-a-half film because the poison sets up a craving in our bodies. We hurry to the lobby and drag a few deep, frenzied puffs.

We catch the train on a crowded night and would rather stand in a stinking smoking-car than sit down with the non-smokers.

We go to a party and find that we can't chat for ten minutes without lighting up. So we smoke ten cigarettes between 10 p.m. and midnight, and wake up the next morning with sludge in our mouths. We rise hacking and spitting, like sick people.

We smoke, sometimes, without even wanting to smoke. We light up without conscious desire. We do it without thinking or feeling.

We switch brands every time a cigarette manufacturer jingles or jangles us with a new dodge—a filter gimmick, a paper twist, an "independent laboratory" chart. We look forward eagerly to the next revolutionary announcement, because each announcement helps us kid ourselves a little more.

That's not a respectable picture, but it explains why we're going to keep on listening to a lot of garbage about filter traps and menthol and porous paper.

Don't you see it now, Roddy? We squares are hooked! We're on and can't get off.

Why don't all the kids let their parents have it at dinner tonight? They can all make the same proposition you did. You kids could start a campaign that just might prove me wrong. I saw an item in the paper the other day that said most kids pick up the smoking habit from their parents. Maybe you kids could pull a switch—by *not* picking up the habit from us and instead shaming us into quitting.

If you shamed or badgered a thousand parents into quitting, maybe ten thousand of us would take heart and give it a try. And then maybe a million adults would go along. And soon—you can't tell—maybe we'd all kick the habit and get our self-respect back.

Love,

Dad

Occasionally vaginal and cervical smears are reported as positive for malignant cells but the biopsy report is negative. Jennings and others (Yates Memorial Clinic, Detroit) describe how frequently this occurs in a series of 12,885 women tested. In this group, 100 were reported as positive for cancer. In 58 of these the biopsy report was positive; in 42 the pathological diagnosis was not confirmed by biopsy during the immediate follow-up period. In 37 of the 42, the cause of the discrepancy was found to be an error of sampling or of interpretation. In the remaining five cases, no explanation was found.

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R. Lee Clark, Jr., M.D., Director and Surgeon-in-Chief of the University of Texas M. D. Anderson Hospital and Tumor Institute in Houston, was installed as president of the Alumni Association of the Mayo Foundation for Medical Education and Research, in Rochester, during the annual meeting of the Association which has a membership of 3227. He was a fellow and first assistant emergency surgeon at the Mayo Clinic from 1935 to 1939. In addition to his many administrative and surgical activities, Dr. Clark is directing medical editor of Texas Cancer Bulletin, an editor of the Year Book Of Cancer and a member of the editorial board of Excerpta Medica.

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A large section of a recent issue of Modern Medicine, (April 1, 1960) is devoted to a symposium -- "Cancer: Current Advances with Clinical Applications" -- which contains ten papers covering the following subjects: trends in cancer research, viruses in cancer, epidemiology, exfoliative cytology, detection and early diagnosis, surgical treatment, radiation therapy, medical and surgical aspects of hormonal treatment, and chemotherapy. Bound reprints of the symposium have also been published.

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Several Divisions of the American Cancer Society, in cooperation with local pharmaceutical societies and druggists, are supplying to physicians prescription blanks carrying on the reverse side the seven danger signals of cancer in the several languages spoken by their patients.

In a "Special Issue" for March 1960, Postgraduate Medicine has published the proceedings of the American Cancer Society's Annual Scientific Session, held in New York last October. The symposium -- "Evaluation of Early Diagnosis of Cancer" -- consisted of the formal presentation of papers and of discussion on the topics: economics of cancer detection, value of periodic examinations in cancer detection, precancerous lesions and their treatment, and treatment of early cancer. Bound reprints containing 26 papers are being made available by the Society.

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The Memorial Center for Cancer and Allied Diseases is offering a Special Fellowship in medical neoplasia to physicians in internal medicine who desire further training in the natural history, diagnosis, complications, pathogenesis, pathologic physiology, pathology and treatment of cancer, with special emphasis on the leukemias, lymphomas and allied diseases. Candidates must be graduates of medical schools approved by the AMA and must have completed, or be in the process of completing, one year of internship. The appointment is for one year, normally beginning July 1, and renewable for one or two years in the case of fellows who develop special interest in a problem under investigation. The stipend is $6,500 per year. Further information may be obtained from Dr. Henry D. Diamond, Chief, Lymphoma Service, Department of Medicine, Memorial Center for Cancer and Allied Diseases, 444 East 68th Street, New York 21, N. Y.

COMING MEDICAL MEETINGS

Date 1960	Meeting	City
Apr. 20-24	International Congress of Gastroenterology	Leiden, The Netherlands
Apr. 25-27	International Academy of Pathology	Memphis
Apr. 25-27	American Proctologic Society	Houston
Apr. 25-30	American Academy of Neurology	Miami
Apr. 26-29	Industrial Medical Association	Rochester, N. Y.
Apr. 28-30	American Association of Pathologists and Bacteriologists	Memphis
Apr. 28-May 1	Hawaii Medical Association	Honolulu
May 1-2	American Society for Clinical Investigation	Atlantic City
May 1-5	Society of American Bacteriologists	Philadelphia
May 2	American Federation for Clinical Research	Atlantic City
May 2-6	American Nurses' Association	Miami Beach
May 2-11	International Conference of Cancer Cytology	Mexico City
May 2-11	Pan-American Medical Association Congress	Mexico City
May 3-4	Association of American Physicians	Atlantic City
May 3-5	Society of Pediatric Research	Swampscott, Mass.
May 5-6	American Pediatric Society	Swampscott, Mass.
May 5-8	Student American Medical Association	Los Angeles
May 7-13	Medical Society of the State of New York	New York City
May 8-12	Radiation Research Society	San Francisco
May 9-13	American Psychiatric Association	Atlantic City
May 11-13	American Association for Thoracic Surgery	Miami Beach
May 11-13	American Association of Genitourinary Surgeons	Dearborn, Mich.
May 12-14	Mt. Sinai Hospital Postgraduate Seminar	Miami Beach
May 15-18	American Society of Maxillofacial Surgeons	Los Angeles
May 15-18	International College of Surgeons	Rome, Italy
May 15-20	National Tuberculosis Association	Los Angeles
May 16-18	American Trudeau Society	Los Angeles
May 16-19	American Urological Association	Chicago
May 16-20	Medical Library Association	Kansas City, Mo.
May 23-28	Asian-Pacific Congress of Cardiology	Melbourne
May 30-June 1	American Gynecological Society	Williamsburg, Va.
May 30-June 2	American Orthopedic Association	Hot Springs, Va.
June 3-8	Pan-American Medical Women's Alliance	San Juan, P. R.
June 5-10	National Conference on Social Welfare	Atlantic City
June 8-10	Canadian Federation of Biological Societies	Winnipeg, Canada
June 8-12	American College of Chest Physicians	Miami Beach
June 9-10	American Geriatrics Society	Miami Beach
June 9-11	Endocrine Society	Miami Beach
June 9-12	American Therapeutic Society	Miami Beach
June 10-12	Society of Biological Psychiatry	Miami Beach
June 11	American Academy of Tuberculosis Physicians	Miami Beach
June 11	International Cardiovascular Society	Miami Beach
June 13-15	American Neurological Association	Boston
June 13-15	Society for Investigative Dermatology	Miami Beach
June 13-17	Canadian Medical Association	Banff, Alberta
June 13-17	International Congress of Clinical Pathology	Madrid, Spain

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